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CONTENTS

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THE AMERICAN
JOURNAL OF PHARMACY

SEPTEMBER, 1919

EDITORIAL.

THE PRESIDENTIAL ADDRESSES.

The pharmacists of Great Britain and the United States are to be congratulated upon the addresses delivered by the presidents of their respective national pharmaceutical associations at the 1919 conventions. The sessions of the British Pharmaceutical Conference were held in London, July 22–23. The address of the president, William Kirby, M.Sc., is devoted almost entirely to a presentation of the need for research in pharmacy. The subject is treated in a masterly manner and the address evidences the careful thought and preparation of a scientific, educated pharmacist who has this subject at heart as well as in mind. As a literary production it, likewise, is a polished gem even among such presidential addresses. As a gem it will bear study and use and the light from its trite truths, so clearly presented, must scintillate and create aspirations that will stimulate scientific investigations among the pharmacists of the English-speaking nations.

The need for the establishment of systematic research in pharmacy is common to both England and the United States and the statements of Mr. Kirby are as applicable to America as to Great Britain and a careful perusal of this address is urged upon all true pharmacists. The necessity for encouraging and fostering pharmaceutical research is plainly set forth as a duty of the government, of the captains of industry, as well as of the colleges of pharmacy.

He quotes the statement that had previously been made in the House of Commons regarding the German organization for research: "In the great chemical works in Germany, for every fifteen men employed in any category whatever there is one highly trained specialist and chemist, and that this industry is so important that

there is one highly trained specialist in chemistry for every forty-five employees in any category right throughout the whole range of industry."

In answer to the query he propounds, What are the reasons we do not trust in science sufficiently to put our money into making the necessary experiments? he advances as rejoinders: "The first is: the average business man knows so little about science that he is totally unable to value its certitudes. Therefore he must have a better and more serious education in it. The second is: our national weakness in believing that when the crisis comes in business or anything else our forceful character will ensure our winning through. Fortunately, English phlegm and courage, and the gift of doing best when things are at the worst, have availed once more to avert a catastrophe. Nevertheless, it is to be hoped that we shall not again handicap ourselves by indulging in such a magnanimous conceit. There is, I venture to think, also a third very important reason for our want of confidence in science as a daily tool. Our science students have not been consistently taught that the flower of the tree of knowledge, of all true science, is research. In other words, for the non-experimentalist, science without research is a jargon, and for the experimentalist a treadmill. The very kernel of all experimental and practical science is to learn how to solve the problems of nature and of art. No science student should be allowed to bear away any diploma or any degree from institution or university who has not spent a useful period in research work in some branch of science."

From the above we are justified in drawing certain conclusions. The American business man is evidently the possessor of the same general characteristics as are depicted for the English man of trade. The English tenacity, courage and "magnanimous conceit" are paralleled by Yankee ingenuity, daring and brag and both are in line for the same educational corrections, to avoid the same pitfalls. We are indeed glad to note the awakening in this respect that is apparent on both sides of the Atlantic Ocean. Many of the colleges in the United States have recognized the necessity for the training of their students in the methods of scientific investigation and research and it is anticipated that the time is not far distant when every university course will require that the graduation thesis of each student shall be an accurate description of some original research engaged in by the student.

Colleges of pharmacy have a duty in thus educating their students, which is imperative, and Mr. Kirby again accentuates the necessity for educating pharmacists on precisely the same lines, as far as physical and biological studies are concerned, as other men who are to be associated with them in research work.

Mr. Kirby is quite optimistic regarding the securing of financial aid for the aid of teachers and others engaged in pharmaceutical research. He says: "Surely means can be devised for the adequate remuneration of teachers and workers undertaking such work. Educated opinion throughout the civilized world is pulsing with a desire to realize the fruits of the tree of science now that it has been discovered by all and sundry. Pharmacy should take its part in this effort to enjoy the hitherto overlooked treasure. Its opportunity is to hand." Pharmaceutical leaders in America add their hearty endorsement to this adjuration and likewise to the project proposing coöperative research in institutions in which botanical, chemical, pharmacological and bacteriological work can be carried out.

The address of President LaWall of the American Pharmaceutical Association is likewise a presentation of subjects worthy of the careful consideration of pharmacists. While it deals, in the main, with problems that are peculiar to the association itself, many of its statements are of general interest to the progress of pharmacy and moreover the correction of defects in the management of the Association or the establishing of new methods and the advanced principles advocated will rebound to the benefit of pharmacy.

The formulating of a national code of ethics to be adhered to by members of the American Pharmaceutical Association will go along way toward the establishing of the profession of pharmacy and answering the uncalled-for criticism that at times are advanced against American pharmacy in toto.

The attitude of pharmacy in the reforms inaugurated by the anti-narcotic legislation and the recent coöperation with the Public Health Service regarding venereal diseases are considered as bearing tribute to pharmacy and as evidences of the true professional spirit by which private gain is subordinated to public welfare.

We are likewise in hearty accord with the presidential statement "that if added responsibilities should come to pharmacists through the issuance of rules and regulations in respect to both alcoholic liquors and narcotics, these should be accepted as a tribute to the dignity and responsibility of the calling and as a recognition of the

honesty and worthiness of the profession as a whole which is implied by such a trust."

Many of the other recommendations of this address of President La Wall are placed before our readers in the account of the meeting of the A. Ph. A. and it is hoped that the thoughts presented in these two admirable presidential addresses will receive the consideration merited and be made effective by appropriate actions.

G. M. B.

FURTHER RULINGS OF THE INTERNAL REVENUE BUREAU CONCERNING NON-BEVERAGE ALCOHOL.

The attention of druggists and manufacturers who are holders of permits to use or sell non-beverage alcohol is directed to the following additional rulings of the Internal Revenue. The efforts of all such holders should be directed toward the elimination entirely of alcoholic beverages or the surreptitious use for beverage purposes of preparations made for legitimate use as medicines, flavoring extracts, or toilet articles. Those who violate the provisions of these acts and regulations or who, as manufacturers or dealers, do not use every effort to prevent such frauds will assume a responsibility which may bring severe penalties as well as reflecting upon the position of the drug trade, every branch of which is endeavoring to eliminate from its transactions all unnecessary use of alcohol and all alcoholic preparations that are consumed as beverages.

G. M. B.

To Holders of Non-beverage Alcohol Permits, Form 737:

The Commissioner of Internal Revenue has ruled in answer to a question as to whether it is necessary for druggists who are already bonded on Form 738 for the use and sale of distilled spirits for other than beverage purposes to file new bonds, prescribed in Treasury Decision 2788, in order to dispense wines and liquors in accordance with the regulations set forth in Treasury Decision 2881, that new bonds should be filed by all persons desiring to handle wines in addition to non-beverage alcohol.

Therefore, all holders of permits on Form 737 desiring to dispense wines and liquors in addition to alcohol, in accordance with the regulations, are required to file new bonds.

TO HOLDERS OF NON-BEVERAGE ALCOHOL PERMITS, FORM 737:

The Commissioner of Internal Revenue has instructed this office to give general publicity to the following statement of the Bureau's policy in regard to the compounding and sale of medicinal and toilet preparations and flavoring extracts:

The general abuses recently discovered in prohibition territory, of preparations manufactured with non-beverage alcohol, indicate that a change is necessary in the Bureau's policy of enforcing the regulation governing such manufacture. Greater precaution must be taken to prevent the marketing, under the guise of legitimate and necessary medicinal and toilet preparations and flavoring extracts, of preparations which do not conform to the standards fixed by regulations, and which are easily and generally diverted to beverage uses. It is not only important that the revenues should be protected in this regard, but also that manufacturers who habitually comply with the regulations and take care that their preparations are not sold as beverages, should not be discredited through the operations of the unscrupulous.

The present regulations (Treasury Decisions 2760 and 2788, copies of which are enclosed) set forth the prescribed standards for all preparations in which non-beverage alcohol may be used.

Hereafter, all manufacturers of preparations in which non-beverage alcohol is authorized to be used will be uniformly held for tax and penal liability where their products have been found to be manufactured and marketed otherwise than according to the regulations. This rule will be followed even though there is no evidence indicating bad faith or neglect on the part of the manufacturer or user of non-beverage alcohol.

Permit holders are therefore informed that all preparations manufactured by them must conform to the standards of the U. S. P. or National Formulary, or Circular 19 of the Department of Agriculture, and to the regulations of the Bureau governing the manufacture and sale of such preparations. It is essential that permit holders through constant supervision and frequent tests, assure themselves that their products are being manufactured according to regulations, and the Department will hereafter hold them accountable. The duty is also clearly upon them, under the law, not only to assure themselves that their products are being manufactured in a legal manner, but that they are not distributed in such manner as to

encourage their use as a beverage. Whenever a preparation is found upon the market which does not conform to the required standards, full tax liability and all penalties, civil and criminal, imposed by the law, will be asserted regardless of the ostensible purpose for which the preparation is made.

Manufacturers, wholesale and retail dealers will similarly be held strictly accountable whenever it is found that the preparations made or distributed by them have been made or distributed under such preventable circumstances as would have assured them, had they cared to ascertain the facts, that the preparations were to be distributed and used as beverages.

THE SIXTY-SEVENTH ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The week of August 25 to 30 witnessed a phenomenal gathering in New York City of those interested in the various pharmaceutical organizations in America. The banquet hall and ball room and the adjacent parlors of the Hotel Pennsylvania offered exceptional facilities for the general sessions of the Association and for the meetings of the various sections, committees and Council of the A. Ph. A. and for the concurrent meetings of the American Conference of Pharmaceutical Faculties, The National Association of Boards of Pharmacy, The National Pharmaceutical Service Association and a conference of the Committee of Revision of the U. S. Pharmacopœia. It was a very busy week for many of those in attendance, as from Monday at 9.30 A.M., when the first meeting of the National Association of Boards of Pharmacy was scheduled, until Saturday afternoon, the program, as arranged, provided for a continuous round of meetings or entertainments and meetings of special committees had to be "sandwiched" with these somehow.

The first General Session of the Association was held on Tuesday afternoon, the convention being called to order by President LaWall at 3.40 P.M. The formalities usually attending such national meetings were omitted and this was one of the few occasions when the American Pharmaceutical Association convened without an invocation to the Supreme Being for guidance and direction of the exercises and deliberations. The letter of welcome from Mayor

John F. Hylan escaped being "received and not read" when one of the members called attention to the fact that such disposition would be construed as scant courtesy. The reading of the letter elicited a round of applause.

The Presidential Address was then presented and referred to a committee of which Prof. T. J. Bradley of Boston was chairman to give due consideration to the recommendations contained and report at the subsequent meeting of the Association. The remainder of the first session was consumed in calling for reports of standing committees and in selecting the all important Committee on Nominations.

A special adjourned general session was held on Tuesday evening, devoted to the presentation for the first time of the Remington Memorial Medal. The presentation on behalf of the New York Branch of the A. Ph. A. was made by Dr. Jacob Diner, whose eloquent and sympathetic tribute to the memory of one whose influence had helped materially in shaping his own career, touched a responsive chord in many of his audience and whose reference to the services that the recipient, Dr. James H. Beal, had performed in behalf of pharmacy, was heartily applauded.

In responding, Dr. Beal read a prepared tribute to Professor Remington, expressing his personal appreciation of the character and services of this distinguished teacher, author and pharmacopœial revision leader. Prior to this function, the surviving "ex-presidents" present at the convention accompanied by the members of their families had a reunion and an informal "Italian" dinner at which it was decided that in order to arrange for the continuance of their duty as a Committee of Award of the Remington Memorial Medal, the retiring president should become automatically the chairman of the committee and the Secretary of the New York Branch should continue as the Secretary.

The reports of the Treasurer, Dr. H. M. Whelpley, and of the Secretary, Prof. W. B. Day, showed that despite the general upset conditions the Association had a successful and prosperous year. Nearly six hundred members were added to the roll. At an early session of the Council, the following distinguished scientists were elected honorary members: Professor L. Guignard, honorary president Paris School of Pharmacy; Professor M. Emile Bourquelot, president Pharmaceutical Society of Paris; Professor Eugene Collin, chemist Central Laboratory for Repression of Frauds, Paris; J. H.

Maiden, director Botanical Garden New South Wales, Sydney; Wm. Kirby, M.Sc., president British Pharmaceutical Conference, and Sir William Glyn-Jones, secretary Pharmaceutical Society of Great Britain.

The various section meetings were well attended and there was no lack of papers or of interest in the numerous and varied topics discussed, the main difficulty being the finding of the time necessary for their proper consideration. This was evidenced, for example, in the forced curtailment of the "Symposium on the U. S. P. Revision" that had been arranged as part of the program of the Section on Education and Legislation.

As a result very largely of the efforts of Mr. Frank H. Freericks, chairman of the A. Ph. A. Advisory Committee for Soldier and Sailor Pharmacists, a War Veterans Section was organized with Dr. R. P. Fischelis as chairman.

No matter what particular interest appealed to the member in attendance, he was sure to find among the papers one or more that presented subjects that contained alike food for thought and profit. If his principal interest was in matters scientific, then the various papers presented at the three meetings of the Scientific Section gave him a surfeit. If, on the other hand, as a practical dispensing pharmacist he was interested in the problems presented by others similarly engaged, he found in the Section on Practical Pharmacy and Dispensing a clearing house for the transmission of such vocational subjects. The Section on Commercial Interest also offered an unusually well prepared list of topics and addresses all of which were of the greatest importance to the adoption of correct business methods that would assure the greatest success. The same can be said with equal earnestness as to the programs of the other sections.

The several recommendations of President LaWall all looked toward improving the service rendered by the A. Ph. A. and the making of this Association a still greater factor in furthering the welfare of humanity. The recommendation that the Code of Ethics be revised and then printed on the application blank for membership, or if that be not possible, that a copy be distributed with each such blank, so that there will be constantly in evidence our professional ideals to which each member is to subscribe, was unanimously adopted. The question of advancing the dues to $7.50 was referred to a referendum vote of the members to be taken along with the annual election by mail.

The Committee on Research was continued with authority to cooperate with other associations planning research work along cognate lines which are based upon service to the profession as a whole or to the public which is the ultimate benefactor. Incidentally, the A. Ph. A. committee on research recommended that the award of the fund available this year be made to George D. Beal, of the University of Illinois, to carry on research on the anthraquinone-containing drugs, and this met the approval of the Council.

The recommendation of the President that laws should be framed covering and regulating the proper dispensing of medicines in hospital practice as such dispensing was equally as important as the practice of pharmacy to the public, was directed to the attention of the National Association of Boards of Pharmacy as one requiring early attention and legislation.

His recommendation that in the selection of delegates to the forthcoming pharmacopœial convention, the Association should be represented by delegates who will attend the Convention and who will be suitable for service on the new committee of revision, was a timely reminder of duty that was favorably received and adopted.

Another recommendation dealt with the subject of a pharmaceutical corps in the U. S. Army and recommended that the American Pharmaceutical Association again place itself on record as favoring the recognition of properly qualified pharmacists by elevation to commissioned rank in a corps affording an opportunity for distinctive service and that the officers of the A. Ph. A. be directed to coöperate fully with all other organizations having the same object in view. The Report of the Committee on Status of Pharmacists in Government Service dilated further upon this subject and advised a continuation of efforts with the Surgeon-General with the hope of ultimately securing the endorsement of the Medical Department of the Army and that a committee of three members be appointed to coöperate with similar committees appointed by other pharmaceutical associations to present to the Surgeon-General the need for modern pharmaceutical service in the medical department of the army and to further the aims of pharmacy in the other branches of the government service. This Committee also urged the endorsement of the bill introduced by Representative Darrow, H. R. 4760, to increase the efficiency of the Medical Department of the U. S. Navy and to improve the status and efficiency of the Hospital

Corps of the U. S. Navy. Also that the Association approve of the efforts to secure improved pharmaceutical service and recognition for pharmacy in the Public Health Service. These several recommendations of the committee and of the president harmonized and were adopted by the Association.

Another recommendation adopted in a somewhat modified form provides that the mail ballots in the future contain opposite to each candidate's name his address and vocation.

Other recommendations adopted provide for the election of an executive committee of the council and as one of the first duties of said committee the searching of the presidential addresses for the past ten years for pertinent suggestions that have been overlooked and which are of present value and importance.

The weather throughout the week was enjoyable, being free from excessive temperature, humidity or severe storms and this undoubtedly added greatly to the enjoyment of the visitors and the spirit that marked every occasion. The entertainments were varied, including vaudeville entertainment, auto ride to the Botanical Gardens and Museum in the Bronx and to other points of interest, the Alumni Luncheon, a composite function participated in by the alumni of all the schools represented with friends and relatives in attendance, a boat ride up the Hudson and then to Coney Island with a coupon ticket to many of the amusements and this topped by a shore dinner at the Balconnades in Luna Park.

The local committee spared neither effort nor expense in their endeavor to make this the greatest and most enjoyable meeting of the A. Ph. A. and their excellent arrangements for both meetings and pleasures added materially in assuring both comfort and benefit for all who were fortunate enough to attend. The sixty-seventh meeting of the American Pharmaceutical Association was certainly a memorable event in the history of American pharmacy and must have a telling effect in its future advancement.

It was determined to hold the next meeting in Washington during the first week in May and just prior to the United States Pharmacopœial Convention.

THE STANDARDIZATION OF PISCIDIA ERYTHRINA (JAMAICA DOGWOOD).*

By Paul S. Pittenger, Phar.D., and George E. Ewe.

Although the amount of Jamaica dogwood prescribed and used by the present-day practitioner is very small as compared with such drugs as cannabis and opium, which possess a somewhat similar but more powerful action, the drug is still used in appreciable quantities.

It is the opinion of the authors that any drug which is worthy of being used as a medicinal agent should be standardized either by chemical or biological methods.

As we were unable to find in the literature any satisfactory method of assaying Jamaica dogwood, we conducted a series of experiments with the object of developing, if possible, either a chemical or a biological method for standardizing this drug.

Since the principal end to be accomplished by the assay of a drug or its preparations is to secure a *means of measuring its therapeutic efficiency,* a chemical method fails of its purpose unless some direct and constant ratio exists between the figures obtained by the assay process and the therapeutic activity of the drug. For this reason it was necessary for us to first develop a satisfactory biologic method for measuring the therapeutic *activity* of the drug. Without a satisfactory biologic method it is impossible to determine whether or not the substance isolated by chemical means bears any relation to the activity of the drug.

We, therefore, first devoted our attention to the physiologic action.

Physiologic Action.

The researches of Ott[1] and Nagle[2] show that Jamaica dogwood possesses a marked sedative, analgesic and hypnotic action.

Of the three actions mentioned, the hypnotic effect presented itself as the most likely means of physiologic standardization.

* Read before the meeting of the Pennsylvania Pharmaceutical Association, Buena Vista Springs, June 26, 1919.

[1] Ott, Isaac: *Therapeutic Gazette,* 1883, supplement to March number, pages 12 to 17 inc.

[2] Nagle, A. C.: *Druggists Circular,* Feb., 1881, p. 18.

The similarity between the actions of Jamaica dogwood and cannabis suggested the possibility of employing similar methods of standardization.

A fluid extract of the drug was accordingly administered in capsules to dogs and found to produce incoördination and ataxia similar to that produced by cannabis.

The hypnotic effect of Jamaica dogwood, however, was found to be less than that of cannabis, as it required approximately 17 times as much Jamaica dogwood to produce the same degree of incoördination in dogs as that produced by cannabis.

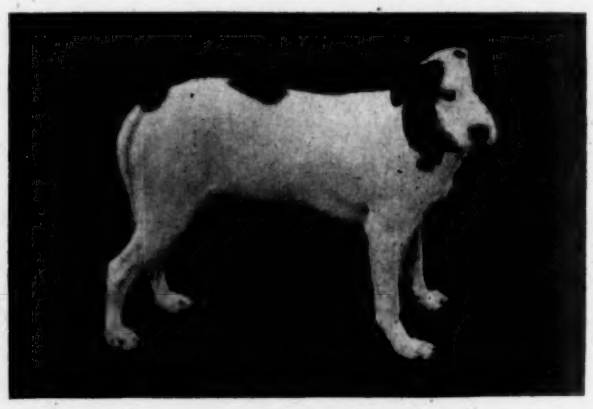

FIG. 1. Normal Dog.

For standardization purposes the end reaction to be observed is one just sufficient to produce muscular incoördination in a dog.

The details of the method employed follow:

Animals.—Short-haired dogs of medium size (6 to 12 Kilos) are well adapted for this work. They show the different stages of the drug's action because of their comparative high cerebral development.

Animals for assay purposes should be selected with great care, it being necessary to pick out those that are healthy, intelligent, quiet, and which have shown by previous tests that they are easily susceptible to the action of the drug.

After several dogs have been selected, the operator, before using them for actual work, should study each animal in order to familiar-

ize himself with the behavior, peculiarities, etc., of the dog under normal conditions. The same animal may be used many times, provided that twenty-four to thirty-six hours are allowed to elapse between doses in order that the animal may *completely* recover from the effects of the previous dose.

Although the animals never appear to lose their susceptibility, it is not advisable to use a dog for more than six months, and care should be taken to allow one week to elapse between assays.

Preparation of Experiment.—Select and weigh several animals which have been found easily susceptible to the action of Jamaica dogwood, and withhold all food for at least twelve hours previous to the time of administration of the drug. Water should be allowed.

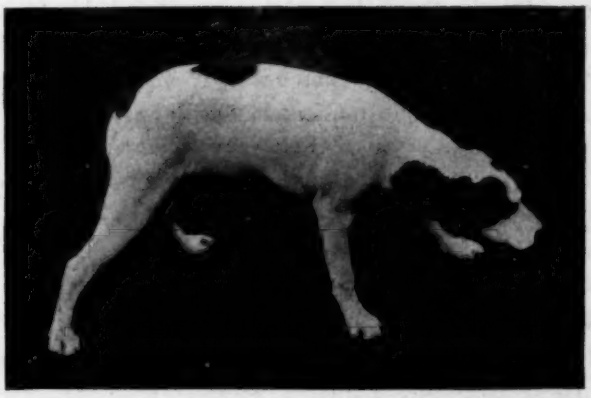

FIG. 2. Same dog as shown in Fig. 1, one hour after receiving a dose of active Jamaica dogwood. This figure clearly illustrates the stage of incoordination produced by Jamaica dogwood. That the dog has lost control of the hind legs and of the muscles supporting the head can be noted by the drooping of the head and hind quarters. Also note that the legs are spread apart in order to maintain balance.

Preparation of Drug for Administration.—Tinctures, solid, powdered, and fluid extracts, are weighed or measured directly into hard gelatin capsules. When a crude drug is to be tested a representative sample should be finely ground and then made into a fluid extract.

Method of Administering.—The drug is administered internally by means of a small capsule. The animal's mouth is opened by

forcing the thumb and index finger of the left hand between the jaws, neck and teeth. The capsule is then placed on the back of the tongue with the right hand and the mouth quickly closed; while still holding the mouth shut, the animal can be made to swallow the capsule immediately by slapping it on the throat.

Actual Standardization.—Administer to a series of three selected dogs 9/10, 10/10 and 11/10 of the standard dose of the preparation to be tested, for each kilo body weight of animal. The animals are then placed in a room where they will be undisturbed and are remote from noise and excitement; careful observation should be made and the results recorded during four or five hours.

If this preliminary test shows that the drug is either above or below standard strength other dogs are given progressively increasing or decreasing doses, as the case may be, until the smallest dose per kilo body weight is found which will produce an action just sufficiently pronounced to bring on the stage of incoördination. This is distinguished by a slight ataxia when walking and a drooping of the head and gentle swaying of the body while at rest. The relative strength of the preparation tested is then computed between the "minimum dose" and the "standard minimum dose" by simple proportion.

The personal equation plays an important part in this assay just as in cannabis, since the accuracy of the test depends largely upon the experience of the operator and his ability in determining just when the effects of the drug manifest themselves. In the hands of an experienced operator, therefore, results may be obtained which will show, with fair accuracy, the relative value of any preparation of Jamaica dogwood.

Tentative Standard.

In order to determine the average amount of the drug per kilo required to produce incoördination in dogs and to set a tentative standard for assay purposes, ten different samples of fluid extract obtained from the various pharmaceutical manufacturing houses in the United States were assayed by the above method and were found to produce incoördination in dogs in the following doses:

Sample No.								
1	0.7	Mils	per	k.	body	weight	of	dog
2	0.6	"	"	"	"	"	"	"
3	0.5	"	"	"	"	"	"	"
4	0.4	"	"	"	"	"	"	"
5	0.7	"	"	"	"	"	"	"
6	0.5	"	"	"	"	"	"	"
7	0.4	"	"	"	"	"	"	"
8	0.4	"	"	"	"	"	"	"
9	0.5	"	"	"	"	"	"	"
10	0.5	"	"	"	"	"	"	"

You will note, therefore, that the average of the above ten samples is 0.52 Mils per k. We have, therefore, adopted the following tentative standard:

"Fluid extract of Jamaica dogwood should be of such strength that it will produce incoördination in dogs in doses of 0.55 Mils per kilo body weight of animal and should not produce incoördination in doses less than 0.5 Mils per kilo, the drug being administered by capsule after fasting the animal for 12 hours.

FIG. 3. Another view of the same dog as shown in Fig. 1, one hour after receiving dose of Jamaica dogwood. This figure shows the animal when severely affected. Note that the legs are spread apart in order to maintain balance, also the drooping of the head and the bowed back.

The above experiment also shows the wide variation in the strengths of the commercial preparations on the market and proves the necessity for standardizing preparations of this drug.

Chemical Investigation.

The only physiologically active constituent which could be found credited to Jamaica dogwood in this investigation was the crystalline substance "piscidin." Piscidin is credited by Berberich[3] as having the formula $C_{29}H_{24}O_8$. Berberich also states that Edward Hart[4] by treating the fluid extract of the bark of Jamaica dogwood with slaked lime, obtained a crystalline substance, which he considered to be the active principle of the bark. The crystals separated on the sides and bottom of the flask, in which the experiments were conducted, after the mixture had stood for two or three days. The crystals were accompanied with a resinous substance. They were purified by recrystallization from alcohol and were finally obtained in a nearly colorless condition. After repeated crystallization from alcohol, the substance was obtained in the form of small yellowish crystals, which, under the microscope appeared to consist of four- to six-sided prisms. Hart further described the crystals as "insoluble in water, slightly soluble in cold, much more in boiling alcohol, only slightly soluble in ether and easily soluble in benzene and chloroform. It is dissolved by strong hydrochloric acid and sulphuric acid and precipitated from these solutions, apparently unchanged, by water. Fehling's solution failed to detect glucose or sucrose. The alcoholic solution is neutral to litmus. Alcoholic lead acetate solution does not produce a precipitate." Berberich found crystals of piscidin to melt at 192° C. and that they conformed to the formula $C_{29}H_{24}O_8$ by elementary analysis. He named the substance "piscidia." Berberich repeated the experiments of Hart. He made a fluid extract from 500 Gms. of the bark by use of 78 per cent. alcohol. The extract was concentrated by distilling off the alcohol until about 100 Mils of liquid remained. This liquid was poured into a beaker containing 30 Gms. of quicklime which had previously been slaked with enough water to make a thick paste. The milk of lime and concentrated extract were intimately mixed, the mixture was allowed to stand in a warm place for one half hour, strained and the residue pressed. The liquid was then filtered. Water was added to the clear filtrate until slightly turbid. After

[3] Berberich, Herman: American Journal of Pharmacy, Sept., 1898, pp. 425–427.

[4] Hart, Edward: *American Chem. Journ.*, 1883, p. 39, also *Therapeutic Gazette*, 1883, pp. 97, 98.

two or three days, crystals separated upon the sides and bottom of the beaker. They were accompanied by a resinous substance from which they were purified by recrystallization from alcohol. By adding water to the mother liquor a second crop of impure "piscidia" was obtained. These purified crystals possessed all of the properties assigned to "piscidia" by Hart.

We have repeated the work of Hart and Berberich with the exception of the melting point determination and elementary analysis and have obtained the same results noted by them.

A modification of the lime method of isolation of piscidin was developed in the hope that it might be applicable to the assay of fluid extract of Jamaica dogwood by chemical means. The details were as follows: 100 Mils of the fluid extract were placed in a centrifuge bottle which had been tared with 10 Gms. of U. S. P. slaked lime in it. The bottle with its contents was weighed to obtain the weight of the sample and the bottle was stoppered and allowed to stand with frequent agitation at 40–50° C. for a half hour. The bottle was then centrifuged and as much of the clear liquid as possible was removed and filtered into a tared 250 Mils Erlenmayer. The Erlenmeyer was weighed to obtain the weight of the sample. The sample was diluted with 3½ times its weight of freshly boiled and cooled distilled water. The Erlenmayer was then corked well and allowed to stand at room temperature for three days with occasional agitation. The crystallized piscidin was filtered off on a tared Gooch, washed with 15 per cent. alcohol and dried at 100° C. to constant weight. Some of the piscidin adhered tenaciously to the flask, so the flask was weighed to obtain the weight of the adherent piscidin, which was then added to the weight of the piscidin found in the Gooch.

Dilution of the aliquot with 3½ times its weight of water was decided upon as yielding the maximum proportion of piscidin, as shown by the following experiments on one fluid extract:

Experiment No.	Aliquot.	Water Added.	Piscidin.
1	50 Mils	50 Mils	0.182 Gm. per 100 Mils
2	" "	175 "	0.219 " " " "
3	" "	500 "	0.220 " " " "

The piscidin yielded by this process is contaminated by resinous matter. Separation of the piscidin and resin was attempted by

means of solvents but without success. Recrystallization of the piscidin from alcohol resulted in purification of the piscidin but this method is not applicable quantitatively to the small amounts obtained in an assay process.

In order to ascertain the relation of the piscidin recovered by this process to the activity of the fluid extract from which it was obtained, the amount of piscidin yielded by 100 Mils of a fluid extract was redissolved in hot alcohol, then diluted to 100 Mils with the weakest strength alcohol which would keep the piscidin in solution and this solution was then tested physiologically in comparison with the original fluid extract. In two experiments the piscidin recovered by assay represented 55 per cent. and 62.5 per cent. respectively of the activity of the fluid extracts.

Ten samples of fluid extracts representing all of the larger pharmaceutical manufacturing houses in the United States were assayed by this lime process in comparison with the physiological assay process in order to determine whether or not the piscidin content paralleled the physiologic activity. The results of these assays follow:

Sample No.	Chemical Assay.	
1	0.219 per cent. impure piscidin	0.7 Cc. per kilo.
2	0.235 per cent. " "	0.6 Cc. " "
3	0.450 per cent. " "	0.5 Cc. " "
4	0.460 per cent. " "	0.4 Cc. " "
5	0.507 per cent. " "	0.7 Cc. " "
6	0.620 per cent. " "	0.5 Cc. " "
7	0.620 per cent. " "	0.4 Cc. " "
8	0.650 per cent. " "	0.4 Cc. " "
9	0.670 per cent. " "	0.5 Cc. " "
10	0.680 per cent. " "	0.5 Cc. " "

These comparisons show that the piscidin content is not in direct ratio to the physiologic activity and therefore make evident the impossibility of using the lime method of isolating piscidin, as a means of chemically standardizing Jamaica dogwood preparations. We have made some experiments with the view of employing lead subacetate in place of lime but the recovered piscidin is likewise contaminated with other substances, but to what extent is not known at present and will be reported upon in a later communication to this Association.

Conclusions.—The result of these experiments would tend to prove, therefore, that we are without a reliable chemical means of accurately standardizing Jamaica dogwood preparations but that they can be accurately standardized by physiological means as outlined in this paper.

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THE USE OF ANIMALS IN THE DEVELOPMENT AND STANDARDIZATION OF MEDICINAL PRODUCTS.[1]

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"The Meyers bill, just introduced in Congress, making it a crime to vivisect the dog, carries into the open and vociferous forum of public debate a question that has disturbed the friendly relations of doctors and dog-lovers for decades.

"There are all shades and degrees of opinion on the subject, all coming at last to the prime consideration of whether it is right under any circumstances to endanger, or take the life of one living being for the sake of another.

"So many of the sound principles of modern surgery have been established by experimentation on dogs, cats, monkeys and other animals, to the very great benefit of human beings, it will be rather hard for the anti-vivisectionists to hold their ground, particularly if they are still eaters of chops from the innocent lamb and steaks from the cunning calf."[2]

In searching for a logical reason for the animus against vivisection one must conclude that it is based on one or the other of two ideas: first that the use of animals in colleges and research laboratories, is unnecessary and avoidable; second, that such use of animals is needlessly cruel and inhuman.

[1] From the Research Laboratory, Parke Davis & Co., Detroit, Mich.

[2] Editorial, *The Detroit Journal.*

Regarding the first of these it should be sufficient to point out that while many of the valuable medicaments were undoubtedly discovered and their values determined by observation of their effects on humans, research men are not now so favorably placed; it is rare indeed when one can find a person willing to be the first on whom a substance which may or may not be a therapeutic agent, shall be tried. The risk is too great, for the toxicity may be greater than its medicinal value.

Regarding the second of these, while in some cases a preliminary anesthesia is not possible, in a large percentage of the cases where animals are employed for ascertaining the effect of a drug, the observation can be made much more carefully, and more accurate deductions drawn if the factor of pain be excluded entirely.

It should be noted further that the use of animals in research is always with the hope of learning facts which will be helpful in relieving pain or saving lives, either human or animal.

This cannot be said of the great destruction of animal life by hunters and trappers who wound or kill for pleasure and only incidentally for profit; a profit which is almost always personal.

It cannot be said of the slaughter of animals for food, since animal food is not essential to life.

It cannot be said of the slaughter of animals for bounty, since in many cases the losses caused by certain animals on whose head a price is set is less than those losses due to an abnormal increase in the numbers of other predatory animals which had formerly been their prey.

Another point not to be overlooked is that in some cases, notably that of using dogs, the demand for research uses rarely equals the supply of undesirables which would have been killed with no useful return, while in other cases, such as guinea pigs, rats and mice the normal supply must be constantly augmented by intensive breeding, in order to meet the demand for research and testing purposes. The use of dogs is therefore no economic loss, and the death no more painful in general than the form of death decreed by the municipality.

General statements, such as those made above, are of little value in combating the untruths and half truths of the anti-vivisectionist. In no other way than by a general investigation can the falsity and absurdity of many of their statements be established.

It has seemed best to meet the situation by a history of the de-

velopment of certain products, and the methods of testing, together with an emphasis on the value to the world, on the one hand, of an intimate knowledge of the properties of medicinal substances, and on the other hand, the benefit resulting from accurate knowledge of the life processes in health and in disease. One must start with certain premises such, for example, as these:

That some medicinal substances are valuable for relieving pain or prolonging life; that other valuable agents may be discovered or developed, substances possibly more valuable than those with which we are familiar; that most human lives are more valuable than the average animal's life. It follows, therefore, that almost any number of animals might be used in developing a remedy for tuberculosis, for example, which, in the U. S. alone, has a toll of 150,000 lives yearly.

There is still another side to the picture—the saving of animal life. Hog cholera in one year, in one state of the Union, caused a loss of nearly 3,000,000 hogs, while one hog, when hyperimmunized with the virus, will supply serum sufficient to immunize 100 hogs.

The disease of rinderpest in South Africa has been practically exterminated by following the information gained from animal experimentation. It is a disease from which hundreds of thousands of cattle died annually, but the antivivisectionist sees only the rabbits that were inoculated to study the disease and the remedial measures, while the suffering and death among millions of infected cattle is overlooked.

What is the answer? What of experiments to eliminate Texas fever in cattle, white scours in calves, chicken cholera, dog distemper? When a disease causes an economic loss and waste of valuable life, experiments are undertaken to eliminate or control the disease, whether it is human or animal life. Vivisection in its broader application therefore saves the lives of thousands of animals to one that it takes.

Antitoxin for diphtheria required the use of a large number of animals before it was perfected but its use has reduced the mortality from over 80 per cent. to under 20 per cent. of those attacked. While in some cases improved hygienic measures may be equally responsible with the remedial agent for a lowered death rate, there is, practically, no other treatment for diphtheria than the administration of antitoxin.

In preparing antitoxin by developing it in the horse's blood, a certain number of horses are valueless for this purpose because the immune bodies will not develop or will acquire only a nominal potency. How is this to be determined? On your child or mine? Or is it more humane to standardize the serum on guinea pigs and by this means eliminate antitoxin of low potency which is indistinguishable from a potent sample by any known test except that on the living animal or human being?

Recently in the daily press, we read of the men who, in the interests of the army as a whole, served as a means of demonstrating whether or not trench fever is transmissible by "cooties." While this disease may not be regarded in the same category as some, during the war it involved discomfort and possible death to many a soldier. This method of study was necessary because it is impossible by animal experiment to demonstrate the correctness of the theory.

The world proclaims as a hero the physician who risks his life to verify certain facts, such as the transmissibility of yellow fever and malaria by the bite of the mosquito. If it were possible to substitute the life of a dog or a horse for that of the man with equal benefit to the world, would it be difficult to choose? The average person would say that the physician was the more valuable to the community and the world.

The natives of Africa were able to make their weapons more effective by dipping the arrow points into a poison prepared from certain seeds, finely ground, and partially extracted. Careful study of this poison on animals revealed the fact that it has a peculiar effect on the heart, causing, in sublethal doses, a slowing and strengthening of the heart beat.

In certain cardiac diseases, where the pulse is weak and rapid, it is logical to use strophanthus, the arrow poison, to counteract the abnormal condition. No statistics could be collected to show the value of this remedial agent, discovered by the hunter and developed by the pharmacologist, the vivisector, but its constant use indicates its importance. To-day, although its place is secure as one of the most valuable of the heart tonics, strophanthus still exacts a certain toll of lives? Why? Because the physician prefers that some almost worthless frogs should die than that he should use an overdose of this powerful drug.

One of the most valuable phases of animal experimentation is the elimination of harmful and of valueless drugs, giving the physician greater assurance of obtaining the desired results from administration of remedies. From this also has resulted the substitution of the pure principles for the crude drugs and nauseous extracts previously used.

It is a common occurrence to find on the market strophanthus seed, as low in activity as one fourth that of the adopted standard and, on the other hand, two or three times as active as this standard. An under dose as, for example, a dose from a sub-standard preparation, might be harmless, but if a life were hanging by a thread and required a dose of an active heart stimulant, either a highly potent or a worthless sample would be equally fatal. In the one case, the worthless sample would not stimulate the heart muscles to the necessary activity. In the other, an extract of an exceptionally potent lot of drug would poison the heart by overstimulation and just as surely cause death.

Ergot is another illustration of this. It has been used for centuries in aiding childbirth and arresting hemorrhage, but has suffered often from the fact that it is uncertain in its action, some extracts being apparently devoid of any action on the uterus. Within my memory, a German chemist put on the market the supposedly active principle called clavin. This substance might be tested in two ways, either in cases of labor on human subjects, or by a few careful tests on anesthetized animals. Two or three tests by the latter method were sufficient to show that clavin was quite inert.

Further chemical, combined with pharmacological, investigations established the fact that ergot owes its therapeutic value to three active principles each of which has its well-marked effect and each of which is equally essential to the complete action of the drug. Without animal experiments carried out in connection with the chemical investigations the composition of ergot and its rational use would still be uncertain. Even with our present knowledge of its composition we are still unable to standardize extracts of ergot except by a physiological test. The usual test applied, however, does not involve death, anesthesia or even suffering except the prick of the hypodermic needle.

The uncertain effects of extracts of cannabis indica, before physiological experiments established the fact that this is due to

variable quality, almost discredited the drug as a therapeutic agent. The question may logically be asked why chemical tests should not be applied to standardize medicinal substances. In reply to this, it may be sufficient to say that pharmacologic standardization (vivisection in one of its broader aspects) is applied only where the active agent is of such a character that chemical tests cannot be applied. It is a more expensive and a less accurate means of standardization and in no case will be retained after an accurate chemical test has been developed.

Pellagra, scurvy, beri beri and some other less well-marked diseases of undernourishment, have to a large extent, been of necessity studied on human subjects. In that way observers have learned that certain foods are essential but that certain forms of food seem deficient in nourishment. In one historic instance a group of Dr. Goldberger's assistants—16 in all, of whom 13 were physicians—voluntarily submitted themselves to experiments in order to demonstrate whether the symptoms of pellagra could be reproduced by any method of infection. The materials used were blood, nasopharyngeal secretions, epidermal scales from skin lesions, urine and feces. These were administered by injections, by application to the muscosa of nose and pharynx, and by mouth. The evidence while negative led to the conclusion that the disease is one due to faulty diet. Assuming that a corrected diet will eliminate one of the worst scourges of the South, who will deny that these physiological experiments were worth while? On the same principle and even with greater humaneness, the use of animals is to be commended wherever such use is possible.

The development of vitamines is another triumph in which physiological studies have suggested the introduction of a valuable therapeutic agent. By experiments on pigeons, rats and guinea pigs, it is possible to demonstrate a life process which could be only inferred from observations on humans, to prove that certain foods are deficient although supposedly containing all the essential constituents. In scurvy, the lacking factor is found in certain fresh foods or in lemon or lime juice; in pellagra, it is apparently in part the substance in the shell or germ of the corn which is removed in milling; in beri beri, it is a loss of the substance removed in polishing rice, or in certain conditions occurring when foods are prepared.

In humans, the disease is slowly developed and responds only

slowly to treatment since it is usually complicated by accompanying pathological processes not directly connected with the disease. In pigeons, on the other hand, the condition of polyneuritis can be developed in a remarkably short time by a diet consisting largely of polished rice, while the recovery from this condition takes place in only a few hours when an extract of the polishings of the rice or, better still, an extract of yeast is administered. The chemical characteristics of these various therapeutic agents are as indefinite as the exact status each has in nutrition, but the deficiency of each of them in the diet can now be recognized and remedial agents suggested, based on the experiments conducted by a number of prominent physiologists as Funk, Eijkman, Veddar, Hopkins, Goldberger and many others. The possible value of this work in recognizing and overcoming disease due to nutritional deficiencies is immeasurable.

Koller, an ophthalmologist of Vienna, in 1884 tested the anesthetizing properties of cocaine on guinea pigs, rabbits and dogs. After noting that in these animals the eye could be touched or scratched without pain after a 2 per cent. solution had been dropped into it, he tried the same solution on man and thus was introduced into medicine a new method of relieving pain and permitting of operations, previously unendurable.

Cocaine is an exceedingly valuable local anesthetic, but it is highly toxic and has besides a habit-forming action which greatly restricts its use. As a result of a careful chemical study of its composition and structure combined with pharmacological experiments on animals, it has become possible entirely to eliminate this drug as a local anesthetic substituting a substance almost equally efficient but at the same time much less toxic and with no habit-forming effects. This in itself would justify the practice of vivisection.

In many surgical operations, profuse bleeding is almost unavoidable, even with the utmost precautions. Further, there are many individuals whose blood is very slow in coagulating and with whom an operation is regarded as almost surely fatal. By the aid of animal experimentation and from the blood and tissues of other animals, substances have been produced which when introduced into the circulating blood shorten its coagulation time so greatly that the danger from excessive hermorrhage has been largely eliminated even in those cases known as hemophiliacs.

Without vivisection such results could scarcely have been obtained. The dog, the horse, the cow and the goat contribute to this valuable therapeutic agent. The part taken by the dog is that of test animal to determine whether the active agents are present, since no known chemical test will show whether they are present in an active form. The dog is, therefore, no less essential in the cycle of operations than the other animals employed. There is no apparent reason why the dog, especially the stray, which spreads disease, contracts and transmits rabies, kills sheep and is rarely useful, should be protected, while an open season exists for deer, quail and trout, and there is no closed season for many animals more deserving of protection.

The animals mostly used in pharmacologic experiments—vivisection, if you please to call it that—are the frog, mouse, rat, guinea pig, rabbit, dog, cat and monkey. Of these, the frog owes its value to the fact that being a cold-blooded animal, its isolated tissues survive a considerable time and can therefore be used, for example, for the study of muscular contraction and the function of the nerves. The guinea pig, rat, mouse and rabbit are chiefly of value for inoculation experiments; while the cat, dog and monkey are useful particularly for experiments on the brain, central nervous system and circulatory system.

The dog is especially valuable in nutrition and digestion experiments because of its diet, which is as omnivorous as that of man. For many purposes no other animal can be used on account of the size of the organs and the convenience of handling. For blood pressure experiments in studying the heart tonics of the digitalis series, standardizing extracts of the pituitary and suprarenal glands, testing the efficiency of hemostatics and blood-coagulating agents, standardizing hypnotics, such as cannabis indica, chloral, chloretone and similar substances, no other animal is so well adapted and from no other animal can the results be transferred directly, almost without alteration, to man.

Where pain would accompany the experiment and when this point is not the subject of the experiment, a preliminary anesthesia with chloretone is usually applied. This general anesthetic can be given internally by mouth and is often so used. Complete anesthesia, recognized by the absence of reflex when the pupil is touched, results in a half hour. Anesthesia remains complete, when the proper

dose is used, until death, the animal being killed at the end of the experiment by a lethal dose of digitalis.

There are certain historical cases where animal experimentation did not precede human use, as for example, Sir Robert Christianson, who almost died from eating Calabar bean from which physostigmine comes; Koeppe, who tried the effects of digitoxin on himself with like result. Chloroform and prussic acid were also investigated with equally unpleasant results. In some cases deaths have occurred, particularly in cases of infectious diseases.

Animal experiments were used to explain caisson disease and suggest means for its prevention and remedy, animals being subjected to air pressure and the pressure applied and released under varying conditions. Such experiments have also made possible the surgical operations which have done so much to relieve pain and prolong life, the human being having the benefit of experience and skill gained by operations on animals.

While physiological experimentation and the standardization of drugs requires the use of all the animals mentioned, the dog is more widely used and is almost beyond replacement. Everyone, almost without exception, regards the dog as a highly intelligent animal, a fit companion for man. There are few dogs used in research laboratories that would have the appeal of Mark Twain's "Tale of a Dog" or that would be welcomed by any but the small boy. The class of dogs used in experiments, picked up by the dog-catcher and not redeemed, is almost without exception friendless. Even the antivivisectionist would at most feel only pity for it and with proper recognition of the use to which it is put would probably realize that in a remarkably few cases is any cruelty involved in using it as a test animal.

Most people will agree with Darwin in saying that "cruelty to the lower animals is worthy of detestation and contempt." But what is cruelty? The transportation and preparation of animals for food, the method of slaughter, hunting, fishing, trapping, are often cruel to an extreme. But they are not condemned. More actual cruelty is probably practiced in this way in a season than occurs in all the research laboratories in the world, in a year. Can vivisection be condemned and sport exonerated?

The advancement of knowledge, the mitigation of misery and the prevention of disease are surely infinitely higher and nobler

motives for infliction of pain, when pain is actually inflicted, than merely healthful exercise and transient enjoyment.

Is it logical, therefore, to attempt legislation to limit and restrict a form of research so valuable to mankind?

NOTES ON THE ASSAY OF HYPOCHLORITE SOLUTIONS.[1]

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Our attention was recently called by Dr. J. W. Sturmer to a difficulty in the assay of a sample of Dakin's solution, in which, after obtaining the end reaction the blue color returned and addition of volumetric solution had to be made repeatedly until a permanent end reaction was obtained.

The Dakin's solution in question was made by passing 4.8 Gms. (or about 1,600 Cc.) of chlorine gas into a solution containing 14.1 Gms. of anhydrous sodium carbonate (or the equivalent of monohydrate or decahydrate) per liter. Should the preparation be too strong it is diluted with a solution containing 1.4 per cent. of anhydrous sodium carbonate.

The chemical reaction involved is

$$2Na_2CO_3 + Cl_2 + H_2O = NaClO + NaCl + 2NaHCO_3,$$

from which can be calculated that 4.8 Gms. of chlorine will require 14.332 Gms. anhydrous sodium carbonate and will yield 5.004 Gms. sodium hypochlorite and also that 14.1 Gms. anhydrous sodium carbonate will require 4.717 Gms. chlorine and yield 4.954 Gms. sodium hypochlorite.

The directions for the assay of the solution are as follows: Measure 10 Cc. of Dakin's solution into a beaker or Erlenmeyer flask containing 50 Cc. of water, add 5 Cc. of a 10 per cent. potassium (or sodium) iodide solution and 2 Cc. of glacial acetic acid. Run in decinormal sodium thiosulphate solution until decolorization is complete, using starch solution as indicator.

[1] Read at the annual meeting of the Pennsylvania Pharmaceutical Association, Buena Vista, June, 1919.

In titrating the Dakin's solution by following the above directions the permanent discharge of the blue color required the repeated addition of sodium thiosulphate and the sum total of the volumetric solution agreed very closely with that required when the 2 Cc. of glacial acetic acid were replaced by 10 Cc. sulphuric acid (10 per cent.) or 10 Cc. hydrochloric acid (5 per cent.). In the latter cases, titration was complete with the first decolorization.

By omitting the water used for dilution, it was found that 2 Cc., or even 1.5 Cc., glacial acetic acid gave a definite end reaction, the results agreeing with those obtainable with dilute sulphuric acid. While the neutralizing power of 2 Cc. of glacial acetic acid is considerably greater than that of 10 Cc. of dilute sulphuric acid (10 per cent.) or 10 Cc. hydrochloric acid (5 per cent.), dilution of the latter does not affect its action, whilst dilution of the acetic acid considerably retards its action. To illustrate—10 Cc. hydrochloric acid (5 per cent.) (equal to 0.8 Cc. glacial acetic acid) or 10 Cc. sulphuric acid (10 per cent.) (equal to 1.2 Cc. glacial acetic acid) will give a permanent end reaction, even if diluted with 50 Cc. of water. 2 Cc. glacial acetic acid (equal to 24 Cc. hydrochloric acid 5 per cent. or 16 Cc. sulphuric acid 10 per cent.) will not give a permanent end reaction unless the 50 Cc. of water be omitted.

The Eighth Revision of the U. S. P. directed the use of 10 Cc. of hydrochloric acid in the assay of Labarraque's solution, while in the Ninth Revision, 5 mils of acetic acid are directed; the substitution of acetic for hydrochloric acid in the assay suggested the possible indefiniteness of the end reaction as noticed in the Dakin's solution.

In titrations made with a deteriorated sample of Labarraque's solution (1 per cent. available chlorine), by the U. S. P. process, several additions of sodium thiosulphate volumetric solution were necessary for a permanent end reaction, but if the quantity of acetic acid was increased to 10 mils the first decolorization was permanent and corresponded to that obtained with diluted hydrochloric acid or dilute sulphuric acid.

The results of the experiments warrant the following suggestions—(1) That the prepared test be allowed to stand one hour before titrating; (2) to increase the quantity of glacial acetic acid to 3 Cc. for immediate titration; or (3) to replace the acetic acid by a diluted hydrochloric or sulphuric acid.

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THE U. S. P. TEST FOR METHYL ALCOHOL IN ETHYL ALCOHOL.[1]

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The U. S. P. test for methyl alcohol in ethyl alcohol having failed to give satisfactory results in the hands of some workers the writer has made a series of experiments to determine the cause or causes of the variable results which have come under his notice.

The fuchsin-sulphurous acid T. S. of the U. S. P. is made by dissolving sodium bisulphite and basic fuchsin in water and adding hydrochloric acid, forming a practically colorless solution.

The test for methyl alcohol is made as follows:

The alcohol is diluted to 10 per cent. by volume, 5 Mils of this are mixed with 2 Mils of 3 per cent. potassium permanganate and 0.3 Mil of sulphuric acid; after five minutes the precipitated manganese dioxide is dissolved by adding sulphurous acid. Then 1 Mil of sulphuric acid and 5 Mils of the fuchsin T. S. "After standing for ten minutes a colorless liquid results" (U. S. P.).

The difficulty has been that when this test was applied to 5 Mils of pure 10 per cent. ethyl alcohol a positive reaction (a violet color) appeared which remained for a long time. It is not considered necessary to describe all of the following experiments in detail, as a summary will be sufficient for the purposes of this paper.

Ordinary U. S. P. ethyl alcohol, deodorized alcohol and alcohol purified by the U. S. P. process for use in making alcoholic potassium hydroxide V. S. were tested with the fuchsin reagent and all gave a positive reaction for methyl alcohol. In all other respects these met the requirements of the U. S. P.

Several samples of fuchsin from different sources were subjected to the U. S. P. tests, but while there was a slight difference in the color given by some on the addition of hydrochloric acid, and one did not decolorize so readily with sulphurous acid, they all gave the same reaction in the test for methyl alcohol.

Elvove recommends cooling the solution after the final addition of sulphuric acid and before the addition of the fuchsin reagent. A

[1] Read before the forty-second annual meeting of the Pennsylvania Pharmaceutical Association, June 26, 1919.

few observations were made upon the influence of the rise in temperature caused by the addition of concentrated sulphuric acid, the solution being cooled to room temperature after each addition of the acid, but the only difference noted was that when cooled the color reaction was somewhat retarded, the final color being the same, and no more attention was paid to the effect of temperature at the time.

Varying the quantity of permanganate solution and the time of oxidation had no noticeable effect upon the final color.

The usual result of the test for methyl alcohol (when applied to ethyl alcohol) was a violet color, appearing more quickly at some times than at others. But one day in making comparisons an immediate bright red was obtained which later faded to yellow, while two days previously the same solutions and reagents produced, more slowly, a violet color. On the first of these two days the temperature was abnormally high and on the last it was lower than usual. The temperature of the laboratory was nearly always above 25° C., so the indications were that these experiments had been made at too high temperatures.

Cooling the solution to 25° C. after the final addition of the acid was again found to be insufficient; cooling after each addition of the acid produced a pale violet color in about 10 minutes, which did not fade when the laboratory temperature was 27°–28° C. When the 10 per cent. ethyl alcohol was cooled to 25° C. before beginning the addition of reagents and cooled immediately after each addition of sulphuric acid and kept at 25° during the oxidation the final result was a negative test. Ethyl alcohol containing 0.25 per cent. methyl alcohol gave a positive test when made at the same time and under the same conditions, but not necessarily within ten minutes. The time required will be referred to later.

Experiments were made in which a more dilute sulphuric acid was used, thus avoiding a great increase in temperature and allowing quicker cooling, but the results were not satisfactory because the red color first produced by the fuchsin T. S. required considerable time to fade. When concentrated acid was used and the solution kept much below 25° a pale red color was produced which in ten to thirty minutes faded to pale yellow in the absence of methyl alcohol, but in the presence of methyl alcohol a violet tint appeared after the red had faded. If the solution is kept at too low a temperature the results are not satisfactory, as the fading of the red color requires too much time.

If the solutions are cooled and kept cool (24°–25° C.) during the test a positive color reaction is obtained provided the methyl alcohol content is about 1 per cent. or higher; but if as low as 0.25–0.5 per cent. the appearance of the color may require from fifteen to thirty minutes, depending upon the kind of light under which it is viewed. With small quantities of methyl alcohol the appearance of the test may indicate a negative reaction even after fifteen to twenty minutes, if viewed by daylight. This is due to a mixture of pale tints which neutralize each other. The final color resulting when ethyl alcohol is tested is a pale yellow, but if methyl alcohol is present the pale violet tint which would otherwise appear is masked by the yellow and the solution appears to be colorless when viewed transversely by daylight, but, viewed vertically, with the light from above, it gradually changes to pale greenish and finally to pale blue or violet. When the same test is observed under artificial (yellow) light the contrast is striking; the source of light may be the ordinary "Mazda" or the carbon filament electric bulb, the open-flame gas burner or even the incandescent-mantle gas light. Viewed directly from above under either of these lights, against a white background, the first indication of the presence of methyl alcohol is a faint salmon-pink color which changes to violet-pink then cherry-red; by reflected artificial light the color is a rather pale violet; the pink to violet may be pale but distinct before any color is perceptible by daylight. These colors relate to small quantities of methyl alcohol (0.25–0.5 per cent.) and require ten to fifteen minutes. With larger quantities of methyl alcohol (1 per cent. or more) the question of light is not so important, the first color being violet and changing to purplish red in a few minutes by either light. Blank tests made on pure 10 per cent. ethyl alcohol may produce at first a pale pink or even a faint violet by artificial light, but if the temperature has been properly controlled these fade to pale yellow in ten to fifteen minutes.

The above figures are approximate, no attempt having been made to determine the exact range of temperature, but the best results were obtained at 23°–25° C. The time required for the appearance of a decided color reaction depends, of course, upon the amount of methyl alcohol present.

Sodium bisulphite is likely to be met with which has a yellowish color and the fuchsin reagent in which it is used may be sufficiently

yellow to make the final test somewhat obscure. A pure sodium sulphite was substituted and the following formula for fuchsin-sulphurous acid T. S. was found to be more satisfactory.[2]

Dissolve .500 Gm. fuchsin in 300 Mils warm water; cool and add 11.2 Gm. sodium sulphite (90 per cent.) dissolved in 200 Mils of water, then add 20 Mils of hydrochloric acid. The fuchsin and sulphurous acid are present in the same amounts as in the official T. S. It has been found best to allow the fresh solution to stand for a few hours before use as it may be temporarily yellow.

It is recommended that the test be carried out as follows:

In the first of two test tubes place 5 Mils of pure 10 per cent. ethyl alcohol and in the second 5 Mils of the alcohol to be tested, which has been previously diluted to 10 per cent.; cool or warm them, as may be necessary, to 25° C. by immersing in water of that temperature for several minutes. Add each reagent to the contents of both test tubes before proceeding further with either one in order to have the conditions in both as nearly alike as possible; cool both quickly to 25° C. after each addition of sulphuric acid and keep them at that temperature throughout the test. If the blank gives a bright red color at once which does not fade in ten minutes, or if a faint pink or violet appears which does not fade in ten minutes, repeat the test with both and vary the temperature. If the blank is violet after ten minutes too high a temperature is indicated; if a bright red color persists, too low a temperature. It is much more simple and quick to make a control test as above than to keep a very exact control of the temperature. In the absence of methyl alcohol no pink or violet color appears within half an hour under artificial (yellow) light, nor a pale greenish, blue or violet in one hour by daylight, the solution being pale yellow or colorless. When much methyl alcohol is present the solution will become violet at once, changing to purplish red.

CHEMICAL LABORATORY OF THE
PHILADELPHIA COLLEGE OF PHARMACY,
June, 1919.

[2] Elias Elvove, "Notes on the Detection of Small Amounts of Methyl Alcohol," *Jour. of Ind. and Eng. Chemistry*, March, 1917, p. 295.

A CHEMICAL TEST TO DISTINGUISH BETWEEN CAFFEINE AND THEOBROMINE.[1]

By Freeman P. Stroup, Ph.M.

Careful study of the properties of caffeine and theobromine has shown that structurally they are, doubtless, very much alike, the chief difference being that in the former a methyl group replaces a hydrogen atom of the latter, resulting in the molecule of the former containing one carbon atom and two hydrogen atoms more than the latter. Otherwise the arrangement of the atoms in the molecule appears to be the same in both. This being the case, the pursuit of any logical plan of testing offered no inducements, and it was decided to go at the task in a purely empirical manner.

Recalling the fact that potassium dichromate and concentrated sulphuric acid properly used produce some striking color effects with certain alkaloids, strychnine in particular, it was decided to try this combination first. The results were both surprising and gratifying. Various proportions of the salt and acid, and various techniques were tried, but the best results were obtained by carrying out the test as follows:

The Reagent.—A solution of potassium dichromate approximately one part by weight in concentrated sulphuric acid twenty parts by volume. It may be made by dissolving 50 milligrams of the salt in 1 mil of the acid, or 3 grains of the salt in 1 fluidrachm of the acid.

The Test: *Technique A.*—Place on a white porcelain surface a small quantity of the alkaloid to be tested (what would lie on the tip of a small knife blade will be sufficient), spread it out to cover a space about 1 centimeter (⅖ inch) in diameter, and put two drops of the reagent in the center of the mass. With caffeine the yellow color of the reagent is almost immediately changed to a bright bluish-green. With theobromine the yellow color is first changed to a dark purplish, which gradually changes to a purplish-green, later an olive-green, and finally to the same bluish-green that is given by caffeine.

Technique B.—Transfer 5 or 6 drops of the reagent to a white porcelain surface, spreading the liquid to form a spot about 2 cen-

[1] Presented at the annual meeting of the Pennsylvania Pharmaceutical Association, Buena Vista, Pa., June, 1919.

timeters (⅘ inch) in diameter, and drop into the center of it a portion of the alkaloid about the size of a grain of wheat. With caffeine the most of it goes into solution promptly, for a moment or two a dark-colored zone surrounds the mass of alkaloid, but in about five seconds this changes to a bright bluish-green, spreading quite rapidly until the greater part of the yellow color of the reagent is changed to green. With theobromine solution takes place much more slowly, a dark-colored zone forms almost immediately, gradually widening until the most of the yellow color of the reagent is changed to a purplish-green, then to an olive-green and finally to bright green.

It will be noticed that in both ways of applying the test the time required for the production of the light green color is very much less with caffeine than with theobromine. This is probably due in large measure to the more ready solubility of the first-named alkaloid in the acid of the reagent.

When used in conjunction with the physical tests for these two substances, given in the dispensatories and other literature, this chemical test should make the differentiation between them a simple and certain matter.

PHARMACY AS A HOBBY AS WELL AS AN INTEREST.[1]

By Charles H. LaWall, Ph.M.,
PHILADELPHIA, PA.

When Bryant said "To him who in the love of nature holds communion with her visible forms she speaks a various language," he uttered a truth which has many applications; not the least of which is pharmacy.

Substituting the word pharmacy for the word nature in the foregoing quotation, gives a clue to the real reason why pharmacy holds its own in spite of commercialism and other handicaps.

There are various motives which impel a man to choose a profession. One, and probably the strongest one, is self-interest. This frequently changes in later life to a realization of opportunity for service and a desire to be helpful to one's fellow-man; motives, which, as a rule, have no place in the make-up of a young man.

[1] Presented at the annual meeting of the Pennsylvania Pharmaceutical Association, Buena Vista, Pa., June, 1919.

By far the strongest and most valuable motive, from the standpoint of the development and progress of any profession, is the one which has to do with the desire for mental development through the acquisition of knowledge.

The answer to the eternal "Why?" has been sought by individuals in all ages and out of this quest has arisen all that we prize in the shape of knowledge. Those who have contributed most largely to the progress of the past are not necessarily the ones who stand out like beacon lights as having enunciated important axioms, or laws, or discovered valuable elements, but the real credit belongs to the silent, patient, plodding workers, who investigate from sheer love of the work and who, little caring whether results have any practical value at the time, store up the material which genius later arranges into that classified coherence which men call Science.

Much of the pioneer work of this kind in chemistry and medicine has been done by pharmacists, whose successors too frequently see themselves frowned upon and discredited by members of both of the sister professions which have been founded and developed through her help.

Much has been written regarding these matters in order to bring pharmacists to a realization of their neglected opportunities. It is doubtful whether any effect has been, or could be, produced in changing the habits of work and of thought of older pharmacists. It is the younger members of the profession in whom the hope of advancement lies and the responsibility for their guidance is largely in the hands of the colleges, for there no longer exists the preceptor of by-gone days who guided the neophyte for a period of three years or more. His disappearance is keenly missed.

One who has his mind so set upon the commercial side of pharmacy as to be oblivious to its history, tradition and possibilities, is not to be swayed, nor perhaps even interested in the following, but it is hoped that it will be read by some of the younger generation and that some will be stimulated thereby to select and encourage such applicants for entrance into pharmacy as betray an interest in the romance and sentiment which are so closely interwoven in its scientific possibilities.

Let us take a brief survey of some of the substances of which medicines are made, with which the pharmacist has more or less frequently to handle.

The tales of adventure, of conquest, of romance, the experiences

of intrepid explorers, of pioneers and colonizers of lands newly discovered, of fortunes gained and lost, of mystery, superstition and witchcraft, of comedy and of tragedy, which are associated with some of even our commonest drugs, would make even a reader who read only for entertainment and stimulation, not for improvement, forsake the most daring writers of fiction.

From the Babylonians, that ancient race of mystery and culture, come the names of some of our most important metals, names by them on account of their fancied association with, or influence derived from, the better known heavenly bodies. Most of these names are only encountered in little used synonyms; as *crocus Martis* for ferric oxide; *sassharum Saturni* for sugar of lead; lunar caustic for silver nitrate; but it is interesting to note that the planetary name Mercury still persists for this most commonly used name of one of our metals, whose compounds are of medicinal importance and value.

Passing along the shelves of any pharmacy and picking out at random from the titles those of more than passing interest, we find one of our best known cosmetic creams, the ointment of rosewater or cold cream, credited as to its origin, to Galen, one of the fathers of pharmacy, who lived at about the beginning of the Christian Era, and for centuries this preparation was called ceratum Galeni.

Galen's influence upon pharmacy and medicine was greater than that of any other single human being who ever lived, or probably will live. His teachings held almost undisputed sway for more than fifteen hundred years, during part of which time, in some parts of the world, pharmacists and physicians were required to pledge themselves to follow his teachings and practice blindly and implicitly.

The names of many others of the preparations and substances used in pharmacy are of interest in their origin and development. Hiera picra means "sacred bitters," evidencing the esteem in which it was once held. Sal ammoniac derives its name from the fact that it was found in the sands of the Lybian Desert near the temple of Jupiter Ammon, resulting from the decomposition of camel urine due to the many caravans which stopped at that point. The influence of the Arabians upon pharmacy may be traced through the nomenclature; the words beginning with al (and sometimes el) being of Arabic origin, as alkali, elixir, alcohol, etc. In the case of the name alcohol the Arabic word means finely divided and was first applied to easily diffusible volatile liquids and finally to the specific substance alcohol.

It is of interest to note that this earlier and original meaning persists in the title "alcoholized iron," a form of metallic iron resembling reduced iron, but prepared by mechanical and not by chemical methods; the word "alcoholized" in this title signifying simply, finely divided, and having no reference whatever to alcohol, as is mistakenly supposed by many who have handled and used it.

The Latin title spiritus vini rectificatus, so long used for alcohol, reminds us of the original source of the alcohol of commerce, which was wine. This title, still found on older shop furniture, is not correct as applied to modern alcohol, which is the produce of fermentation of any saccharine material. That the abbreviation S. V. R. which was frequently employed in former times to designate this substance in hastily written prescriptions, is no longer intelligible, was lately instanced by a student who rendered it, in answer to an examination question, "Service very rapid."

Phosphorus (light-bearer) corrupted into foxfire by country people who see the gleam of phosphorescent decayed wood in a forest on a dark night; antimony (against monks); vitriol (glass like); sal aeratus (gas- or air-producing salt); each of these names alone might furnish material for an article, yet we use them without a thought of their underlying interest and origin.

Of the many synonyms of compound tincture of benzoin, which have accumulated during the centuries in which it was esteemed and used as a vulnerary, Jesuits' drops and Friars' balsam give it a religious association which is distinctly different from the martial thoughts called up by balsam of Maltha, although the Knights of Malta probably used it in the Crusades.

Our common substance sodium sulphate, now almost exclusively used in veternary practice, was discovered in the waters of a European spring by Glauber, a German chemist, whose name appears in its synonym (Glauber's salt) and so highly was it esteemed as a remedy in the early years of its use that it was called "sal mirabile," or the admirable salt.

Red oxide of mercury (erroneously called red precipitate, for it is not made by precipitation) conjures up visions of Priestley working in his home in the Susquehanna Valley with the crude apparatus which he fashioned from glass bottles, kitchen utensils and an old gun barrel, for it was from this substance that oxygen was first evolved by him in amounts sufficient to identify it and study its properties.

Morphine brings to mind Serturner in his little apothecary shop in Eimbeck, Germany, competing, all unawares, with the French pharmacist Derosne for the honor of discovering the first alkaloid morphine (called then vegetable alkali).

When we come to the drugs of vegetable origin we find the greatest opportunity for memory and imagination to run riot as our eyes glance over the list. Opium bringing to mind early morning in dew-kissed fields of snow-white blooms and nodding fruits and of the care that must be taken in incising the outer surface of the capule so as not to lose the drop or two of milky juice that subsequently hardens and becomes what was formerly called meconium, now the opium of medicine and pharmacy. Conium, with its mousy odor, reminding us of the death of Socrates and through that association of ideas of Plato and the other Greek philosophers who enriched our minds and thoughts for all time with their speculations and maxims.

Myrrh, frankincense, cinnamon, cloves, nutmegs and their like, what thoughts of caravans plodding across sandy wastes; of odorous Eastern isles; of fleets of galleys and later of sailing ships, are brought to memory. The trade in spices and precious gums and balsams has been responsible for the establishment of kingdoms and republics of olden times of commercial rivalries more fiercely waged than any of modern times, resulting in the overthrow of dynasties and in repeated changes in the world's map, and this chapter alone is well worth perusal. How many who handle and use nutmegs, with their white powdery coating of chalk, know that this is now a meaningless custom dating from the days when the Dutch, who controlled the spice islands, dipped the nutmegs in milk of lime to prevent their germination, thus assuring a monopoly in their growth and sale for centuries.

It is to the new world that we must turn, however, for some of our most interesting drug histories. Cinchona, a drug of mysterious origin as to the discovery of its properties, for it is not to-day, nor has it ever been, used as a medicine by the natives of the Andean slopes where it is indigenous.

Ipecac, used as a secret remedy for dysentery by a celebrated European physician, whose successes were so great that a French monarch paid him a handsome sum to divulge the name and origin of the remedy.

Sarsaparilla, once vaunted to the skies as a remedy in many

chronic affections, masquerading for years under false colors as to its real value; for both its alleged therapeutic properties and its flavor were due to other drugs used in its combinations; now almost entirely discredited as a remedy of any value.

Hydrastis and sanguinaria, the yellow and red "puccoon" of the aboriginal American, who used them for pigments as well as for their medicinal value.

Boneset, tansy, pennyroyal, horehound, all of these conjure up visions of old-fashioned attics with bunches of dried herbs suspended from the rafters.

Fucus and chondrus bring with them the tang of the sea and of rock-bound weed-strewn coasts, where surging billows want the mariner that Poseidon never sleeps.

With these thoughts singing through one's mind, how can anyone say that pharmacy is decadent, or that it holds no interest for its devotee. There is much and great work yet to be done and discoveries will yet be made bringing to their authors fame and possibly fortune.

Each day's work becomes a miracle to him who looks with seeing eyes into the graduate or mortar, test-tube or flask, and to him who with interested mind draws near to nature's manifestations of her innumerable laws, immutable and sometimes inexplicable. Who is there that has not time to add his quota to the knowledge of his time and of his calling, be it ever so little. Each day some new fact may be learned and recorded; untrodden paths of experimentation lie waiting for generations of pharmacists yet to come. Shall we now pass them by and leave to those of the future our responsibilities in the present?

The studying of colloids, of the sera and vaccines with their fascinating theories and illimitable possibilities; these are subjects in which any pharmacist of the present generation may be as well posted as the foremost savant of the time, for they are of such recent development that one may easily start at the beginning.

If pharmacy sleeps and is not yet aroused to her possibilities, it is time for her to awake, and this awakening will come, when it does come, through a realization of the infinitely interesting possibilities for development along lines of combined scientific and practical value. Let us all join hands in building more strongly for the future, by inculcating in our younger workers that abiding love for and interest in pharmacy which shall outlast all ephemeral consid-

erations of expediency and commercialism, except as absolute necessities. Pharmacy as a hobby adds to the happiness of the individual and can be turned to profit.

ON ADVERTISING.

By Joseph Jacobs,

Atlanta, Ga.

The article by Dr. Jacob Diner on advertising in the July number of the American Journal of Pharmacy, has much to commend it. It shows a real and practical experience with various mediums of advertising, and no drug store which follows the suggested lines laid down will go to trouble in vain.

Regarding newspaper advertising, Dr. Diner was both brief and inconclusive. He suggested that the average drug store could not use the newspaper columns in the larger cities to advantage, because of the great loss in circulation values, that would necessarily result.

This criticism, if made to apply to the corner drug store in the residence section, or a store that has but a limited clientele, is, of course, correct. It is foolish to pay for 50,000 circulation, when it is expected only to reach five or ten per cent. of prospects with a selling argument.

But this must not be applied to drug stores or to any other business that operate in the central commercial district or to those institutions which have branches radiating from a central location. For after all is said on the subject of advertising, the newspaper columns must still hold the supremacy for reaching the people. Dr. Diner admits the power of the press when he advises druggists to watch the news columns of local papers to secure notices of births, in order that postcard greetings may be sent to the new parents. For this and similar reasons, the entire public of a city are constantly watching the columns of the press.

Timeliness of advertising is its greatest virtue; and to the store that has daily or frequent "specials," new trade can always be developed by a well-displayed advertisement in the newspapers. Thousands of people in this day and time do all their buying before they leave home, by picking out from the papers just those things that are listed for which they have need.

But the newspaper will not do away with the need for other mediums of advertising, as Dr. Diner has well shown; and it is with the combined aid of the press, of attractive show windows, of well arranged store interiors, of personal advertising, of special mailing lists and of jam-up service, that the progressive druggist must build his larger success.

THE ECONOMIC VALUE OF THE WHOLESALE DRUGGIST.

In the May, 1918, number of this JOURNAL, page 397, reference was made to the announcement of a prize contest inaugurated by the National Wholesale Druggists' Association, the prizes consisting of various sums ranging from $150 to $20, to be awarded for essays written by traveling salesmen on the subject of "The Economic Value of the Wholesale Druggist and Reasons Why He Is Essential." The committee who acted as the judges in this contest were Mr. Walter V. Smith, of Philadelphia, Mr. J. K. Lilly, of Indianapolis, and Mr. F. H. Garrett, of Council Bluffs. They awarded the first prize, $150, to O. B. Wells, of Albany, the second prize, $100, to H. B. Rhoads, of Indianapolis, the third prize, $50, to H. S. Godshall, of Philadelphia, the fourth prize, $30, to J. F. Beerkle, of Omaha, and the fifth prize, $20, to Joseph Bailey, of Kansas City, Mo.

These prize-winnng essays have been published in pamphlet form and distributed by the N. W. D. A. and well merit careful perusal. The space available permits only of brief abstracts from these.

From the first of these essays the following abstract is given:

"The rôle of the wholesale druggist is of a double nature. His work is for the manufacturer as well as the retailer. He brings to the counters of thousands of retail druggists the products of innumerable manufacturers. Distribution is the keystone of successful business, and the manufacturer finds a quick and inexpensive distributing agent for his product in the wholesale druggist.

"The saving of overhead and selling expense which is effected by the wholesaler for the manufacturer is of considerable importance from the producer's standpoint. It is possible to greatly reduce the selling organization and simplify the credit department. An intricate and expensive accounting system no longer becomes

necessary, for business is done with a single wholesaler whose responsibility is above reproach.

"In the foregoing we have considered the economic value of the wholesaler to thousands of manufacturers. This is an important reason for his existence. Now let us consider his relations to the retail trade.

"One of the great advantages of the wholesale druggist to the retailer is the saving of time. One order placed with the wholesaler brings one composite shipment of assorted goods, that might otherwise of necessity be ordered and shipped from a score or more of houses, some of them at great distance from the retailer. The time saved in ordering and receiving goods makes for a quicker and more satisfactory service, and service is the superstructure of all retail trade.

"Consider, too, the time saved in keeping accounts with a single company instead of a large number of concerns. There is less likelihood of a mistake in adjusting claims, and difficulties of any nature can be settled more readily and with much less effort, if the retailer is dealing with a single company.

"Turnover and quick service are the potent factors in making the retail business a successful enterprise.

"Another point is the advantage to the retailer of the wholesale drug salesman. The 'see you next week' representative of a wholesale concern is of vastly more value to the retailer than is generally realized. In the salesman the retailer has a warm friend. The interest the salesman has in his trade, his good advice, his trade tips on prices, advances, declines, market conditions and what-not make for a splendid cordiality and help to build up an 'over the top' spirit which is bound to win.

"The retailer is not entirely dependent upon his own judgment in placing orders for goods, for the knowledge the salesman has of the goods and demands of the retail trade may be depended upon in those matters. The wholesaler keeps up the quality of goods for the retailer. He makes it his business to make a study of the quality of his goods. Thus the wholesaler and retailer coöperate to give the best possible service to the patrons of the retail trade—the consuming public.

"Every retailer is dependent upon some system of credit in purchasing goods. If there were no wholesale drug concerns the

retailer would very likely be obliged to establish and maintain credit with a large number of manufacturing companies. Such a condition would entail a large amount of clerical work, long delays, misunderstandings and dissatisfaction to all parties concerned. On the other hand, it is a comparatively easy matter to furnish reference and make necessary banking arrangements to do business with one company.

"Another expense which the wholesaler saves the retailer is that of accounting. The bookkeeping necessary when the druggist makes use of the wholesaler can be done easily and without inconvenience by the retailer himself. Thus a great saving is effected.

"So it is obvious that the wholesaler stands to the retailer in the same relation that the retailer stands to the consuming public. He is indeed a necessity, an economic asset, an entity of great importance and great worth."

From the second of these essays the following abstract is given:

"There has been a great deal said and written in the past few years about the elimination of the middle man, or more direct routing of commodities from the producer to the consumer. The term 'middleman' is a misnomer. The proper word is 'distributor,' for that is his function. A great deal of the speaking and writing has been done by demagogues, visionaries and people unfamiliar with trade relations and requirements. Theoretically, it would be a fine thing for the producer to hand his product directly to the consumer and so eliminate the just toll taken by those who would normally assist in its distribution, but in practice it would be, in most instances, an impossibility.

"Considering the volume of business he does, the druggist probably stocks a greater number of items than any other merchant. Every country on which the sun shines contributes to his stock. 'No merchant sells more diversely borne nor more widely traveled merchandise than the pharmacist.' Earth and sea, flora and fauna, raw material and finished product are all found in his stock; and the assembling of the six or seven thousand different items represented in a well-stocked retail drug store, without the aid of the wholesaler, would be a physical impossibility.

"The wholesaler bears the same relation to the retailer that the ordnance and quartermaster's departments bear to an army. When Foch started his offense against the Germans he would never have

succeeded if he had had to replenish his supplies of ammunition, food, etc., from their source; but back of the line were vast stores of these essentials, and as they were needed they were brought up and the guns and the men kept fed. There was never a pause in supplies of materials needed. The men on the firing line knew that what they needed would be at hand when and where it should be. Their time and endeavor could all be concentrated on making use of the material. The retailer is on the firing line and can concentrate on his selling, knowing he can replenish his stock from his wholesaler as he needs the goods.

"No more vital and interesting question confronts the retail druggist than that of turnover. To insure quick turnover the retailer must buy frequently and he can do this only by depending on the wholesaler. Dollars ought to be made to work. A dollar that is not working is a slacker. A retailer that is not working is a slacker. A retailer who turns his stock four or five times a year, if he makes a legitimate profit, will make money. The man who turns his stock twice, or less—and many do no better than this—can not make money.

"The secret of success in selling merchandise is to buy often and get your money back to reinvest.

"The wholesaler, through his connection with sources of supply, comes into possession of information which he in turn passes on to his customers, enabling them to buy and sell to greater advantage. Just since the war began the drug wholesalers of the country have saved their customers thousands of dollars by advising them as to their buying, and impressing upon them the importance of adjusting prices to market values, and enabling them thus to obtain the legitimate profit to which they were entitled. When the retailer is threatened with legislation that menaces his business the wholesaler is always called as 'first-aid.'

"The wholesaler is a clearing house for the things the retailer wants to know. Suppose the retailer were buying direct from dozens of concerns all over the country. No one of them would be sufficiently interested to render this service. And personal service does appeal to the customer. Many druggists could not get along without it.

"In conclusion the wholesaler is essential because he is equipped and organized to render the thing most vital to the retailer—service."

From the third of these essays the following abstract is given:

"The economic value of the wholesale druggist is primarily based on service; therefore, he is essential in direct proportion to the amount of service he renders.

"It is the duty of the wholesalers to serve directly two important classes of business: the producer or manufacturer and the retail distributor, and indirectly the consuming public.

"The large producers of proprietary articles who advertise nationally recognize the fact that thorough distribution is absolutely essential in any advertising campaign to make it successful. The quickest and most economical distribution is undeniably through the wholesaler.

"The facilities of the wholesale druggist mean for the manufacturer: (1) Widely separated distributing points for the manufacturer's goods subject to immediate delivery to cities, towns and hamlets everywhere. (2) The opportunity of connecting up and keeping abreast with an advertising campaign in any section of the country through the frequent visits of the wholesaler's sales force. (3) The responsibility in collecting for the sale of merchandise to the retailer. (4) Concentration and economy in shipping goods to central distributing points. (5) Prompt payment of the manufacturer's bill.

"These are all of them positive and indisputable benefits to the manufacturer.

"For this service, the wholesaler receives a trade discount from the manufacturer's list price and in most instances a discount for prompt payment of the manufacturer's invoice, which is his remuneration for the handling of this class of merchandise, and from which he must pay all his overhead costs of handling the goods and have something left for profit.

"Without the service of the wholesale druggist, the manufacturer would be compelled to do many things: (1) To establish selling agencies in various sections of the country with heavy overhead costs. (2) To employ a large sales force, to cover the entire country, at high salaries, and heavy traveling expenses. (3) To carry many accounts on his books with a high cost of collection. (4) To ship small lots of goods to all sections of the country at a big expense and enormous detail. (5) To have his money tied up in numerous accounts and lose the advantage of ready capital.

"These points make it very clear that the wholesaler derives his profit only out of the saving he affords the manufacturer or producer.

"The wholesaler serves the retailer in many ways: (1) He supplies him with upwards of 2,500 articles in one shipment with little capital outlay, and replaces them at short notice on re-order, giving the retailer the advantage of a frequent turnover; a concentration of freight bills to a minimum cost and he eliminates them altogether if located in the same city. (2) He collects drugs from all parts of the world, guaranteeing quality, freshness and analysis for standard requirements. (3) He extends credit when credit is needed. (4) He facilitates a quick and easy adjustment of claims. (5) He watches the market for new goods and keeps abreast of the times so that the retailer may obtain with dispatch and economy small amounts of newly advertised goods. (6) He maintains a well-posted sales force not only to show and sell goods, but to impart trade information, give advice and keep retailers posted on federal, state and municipal legislation, and to look after his interest in general.

"These are the reasons why the wholesaler is essential to the retailer in the scheme of present-day merchandising, and without him, it seems very clear that chaotic conditions would face the retailer."

From the fourth of these essays the following abstract is given:

"The wholesale druggist is essential, and renders an economic service which is three-fold: he serves the manufacturer, the retailer and the consumer. The wholesaler acts as warehouseman, and is as necessary to the manufacturer as the clearing-house is to the bank.

"By marketing his product through the wholesaler, the manufacturer reduces overhead expenses in all the departments of his business, with the possible exception of the advertising department.

"It is through the wholesaler and his salesmen that the manufacturer gets his product on the shelves of the retail druggist in the city and country, and at a lower distribution cost than he could otherwise obtain. He has no occasion to worry over the collection of accounts, as the wholesaler either discounts his purchases, or pays them at maturity, which is not the case with the average retailer.

"If there had been no wholesalers during war times, a great number of the retailers would have been obliged to close their

doors, as it would have been impossible for them to keep up stocks. As it was, all they had to do was to look pleasant, as their good friend, the wholesaler, did the worrying, and in those days there was cause for it. The average retailer does not appreciate that today the wholesaler has to pay spot cash for much of his merchandise. Nor does he know the amount of money the wholesaler has tied up without a chance of turning a dollar of it over for months at a time. He gives the retailer dating on this same merchandise for which he has to pay spot cash, and all for the sake of rendering an economic service. The retailer certainly could not get this same service by buying direct from the manufacturer or direct-selling house.

"Who kept the retail druggist posted as to all the rapid price changes during the four years and a half of war? advised him what, how and when to buy? kept him informed as to all the new government regulations and rulings that affect his business, in order to keep him out of trouble? Was it the manufacturer—or any of the direct-selling organizations or their representatives? No, it was through the wholesaler and his representatives that he got all of this information.

"And now when business conditions are changing and stock is low and prices declining, the retailer will have to lean more upon the wholesaler than he did before or during the war for the adjustment of his business affairs.

"Statistics show that it costs the retail druggist about 35 per cent. for overhead expense. If there were no wholesalers of drugs, and the retail druggist had to buy everything direct from the manufacturer, it would increase his overhead at least 10 per cent., which would make 35 per cent., on account of extra expense for stock clerks, floor space, increased stock, depreciation, express and freight charges, and many other items of expense, which he does not have to bear in buying from the wholesaler. The ultimate outcome of all this would be that the dealer would have to raise his selling price to the consumer, as the average gross profit for the retail druggist is 33⅓ per cent.

"The wholesale drug salesman is the connecting link between the manufacturer, wholesaler, retailer and consumer. The wholesaler relies upon his salesmen to present his special lines to the retailer and to adjust difficult matters pertaining to accounts, short-

ages, breakage, returns, etc., as the average retailer is a poor correspondent. The retailer relies on the drug traveler to bring him news of events affecting his business.

"Many retailers are not good stockkeepers, and were it not for the presenting of seasonable things in rotation by the drug traveler they would, generally speaking, be buying holiday goods the day before Christmas, and everything else in a similar manner. It is here that the customer is accommodated, as it is through the efforts of the drug traveler that he is able to purchase the latest commodity when he wants it."

From the fifth of these essays the following abstract is given:

"The principle of distribution operates in the normal processes of nature. The elements of bone and tissue in the animal economy, and, in a sense, fluid and fiber in the vegetable, are assembled at a common center from numerous sources and thence distributed to every part. When this process is functioning properly we have health and development, but when interrupted, decay ensues.

"So in the commercial life—particularly as it pertains to the drug business—the same processes are essential to a wholesome condition and a perfect balance.

"The wholesaler himself recognizes the advantage of this process and is in his turn, a patron of other distributors still nearer the source of production, such as the importers and brokers in the remote world markets. He does not purchase his cinchona in the forests of South America, nor his opium in the poppy fields of China. Neither does he visit the factories of France to buy their exquisite perfumes or other rare luxuries of the toilet. These are purchased from importers and others who comb the fields of foreign production and assemble them here at points for convenient distribution.

"This he does because no other plan is practical or even possible. And, for the same reasons, the retail druggist must depend upon a like service through his wholesaler.

"Now if the wholesaler were eliminated and the retailer bought direct, this would mean a separate transaction with each of more than a thousand manufacturers, instead of one wholesale house. It would mean many accounts payable on his books where otherwise one would suffice; the writing of thousands of letters in the course of replenishing stock where now an order given the whole-

saler's representative from time to time will accomplish the same purpose. Then again in remitting these accounts it would mean thousands of letters and thousands of drafts instead of a check now and then to the wholesaler. The postage alone in this infinite correspondence would represent no insignificant sum.

"The same multiplicity of detail and labor extends to all lines in the store. Some idea of what this means may be gathered from the statement that the average wholesale drug house carries over forty thousand items in stock.

"Another advantage that must be appreciated by the retail trade is the regular visits of the wholesaler's representative—the salesman. He is only an arm of the wholesaler's service, but as essentially a part of it as is the buying or the shipping departments. The value of his service can not be over-estimated. Every conscientious salesman recognizes that his acquaintance on his particular territory, and the confidence he commands are valuable assets. He also realizes that the better service the more he increases the value of this asset. Consequently it can be relied upon that he will protect their interests in their relation with his house with the same solicitude with which he would treat his employer's interest in the same transaction.

"I have referred to the sameness of interests between the retailer and the wholesaler. In the fever and confusion of business the significance of this is often overlooked. I do not believe the relations between the retailer and wholesaler in any other line of business are so marked by the same splendid sentiments and unselfishness. The wholesaler stands as a ready champion of the retailer's rights. And it can not be alleged that his motives are always mercenary. There is a willingness to respond to his needs; to coöperate with him in every movement that conduces to better business and higher ideals. This is attested by his efforts to discourage price cutting, to keep down unwholesome rivalries, to secure more favorable legislation, to protect against the piracy of mail-order houses, to obtain from manufacturers a scale of prices permitting a more reasonable margin of profit on advertised products."

APPLIED CRYSTALLOGRAPHY.[1]

By Henry Leffmann, M.D.,
Philadelphia.

Crystals are attractive to the learned and unlearned. The crystalline form of any given substance is always more striking than the amorphous form, gives better evidence of purity and serves far better for identification. Most chemists, however, are not deeply learned in crystallographic lore, whether engaged in teaching, research or analyses in the commercial or works laboratory. The pharmaceutic chemist depends to a limited extent on the crystalline form of the common medicinal salts, but it is the mineralogist who has cultivated the science of crystallography to the greatest extent. The crystals of natural minerals are usually so large and so characteristic as to constitute one of the most important means of identification, indeed, this feature has dominated mineralogy to such an extent that it has become largely a science of external form, rather than chemical constitution. The mathematical exposition of crystals is complex and abstruse. Chemists generally take no interest in it. They do not trouble themselves with the mysteries of the basal pinacoid, hemihedral and tetartohedral modifications or enantiomorphism. This is largely due, of course, to the fact that the chemist deals in the main with artificial substances of which the crystals are minute and imperfect, and even when dealing with a crystal of an artificial substance produced on the large scale and, therefore, presenting distinct form, the practical chemist prefers only to rely on chemical tests rather than optical and geometric methods.

The microscope is much more in evidence in the chemical laboratory than it was fifty years ago, but even now in many of its applications no use is made of the valuable accessory appliances that mineralogists and especially petrologists employ. In clinical, physiologic and toxiologic chemistry most workers are still satisfied to describe the crystal forms that they find in the microscope field by such common terms as "stellate," "needle-shaped," "plate-like." We still hear of the "dumbbell" crystals of calcium oxalate—or oxalate of lime, as clinicians persist in calling it—and of the "coffin-

[1] Reprinted from *The Catalyst.*

lid'" forms of ammonium magnesium phosphate. The different attitude toward mathematical crystallography on the part of chemists as compared with mineralogists is due to the fact, indirectly mentioned above, that the chemist deals with minute forms, with which our sense of touch is not available. The field of the microscope is practically a two-dimensional space, the full appreciation of a crystal requires its measurement in three directions.

Of late, however, a much more extended application of the microscope to the solution of analytic problems has been inaugurated, and in the course of a few years a vast amount of data of the most valuable type will be obtained. For this special training and highly specialized apparatus is required. Thorough knowledge of the mathematics of crystallography, in the phenomena of polarized light and good technical skill are required. Elaborate equipment of the microscope is needed, polarizing apparatus, selenites and similar accessories, practically unknown to the general analyst and works chemist.

The United States Bureau of Chemistry has been for some time carrying out researches along these lines, and has a special worker, Dr. Edgar T. Wherry, to whom the title of "Crystallographer" has been given. As he was a pupil of mine in his elementary studies in chemistry, and as I have been associated with him in work at the Wagner Free Institute of Science. I have had special interest in his researches. At the meeting of the Philadelphia Mineralogic Society in March last, Dr. Wherry presented some of the results of his investigations. Among these was an ingenious detection of an unusual sugar that had been obtained by the bees of a certain area in the United States through feeding on the honey-dew produced by an immigrant aphis. This sugar was not digestible by the bees and they starved to death in great numbers. Another instance of the use of the methods was in determining the reason for the differences in color in a new high explosive which the United States authorities were making. It was found that the differences were due to inclusions in the crystals.

A remarkable application of x-rays to the study of molecular structure has been discovered and some extremely interesting results are already at hand. So far they have a bearing on theoretical questions only, but chemists know very well how soon pure science may be translated into a practical form. Space does not permit of discussion of these x-ray studies.

The invention of simple processes of color photography has been of great assistance in putting on record the appearance of the microscopic field and enabling it to be shown by means of the ordinary projecting lantern. The effects of polarized light are especially brilliant, and the colors are essential in many cases for differentiation. Many members of the section will recall the series of photomicrographs in color that I showed at the summer meeting at Swarthmore some years ago, although the vividness of the demonstration was seriously impaired by the inferiority of the projecting lantern.

A field that seems to promise much, but has not yet been worked to any extent by the chemist, is the use of ultra-violet and infra-red light for differentiation substances. In the case of the former, photomicrography must be used, as the ultra-violet rays are invisible to the human eyes, and very injurious to it.

ANTISCORBUTICS:[1] I.

Ever since Holst and Fröhlich[2] asserted, in 1912, that the antiscorbutic property of certain fresh vegetables and fruits may be to a large extent lost when they are subjected to a high temperature or are dried, students of nutrition have been more alert to the possible effects of culinary processes on some of the less understood properties of foods. Although, as has already been discussed in these columns, McCollum and his colleagues have assumed that scurvy is a disease related to intestinal putrefaction and the retention of feces, the concordant opinion of other recent investigators, notably Givens, Hart, Hess, Mendel, Steenbock and their co-workers in this country, and Chick, Harden and their collaborators in England, has substantiated the earlier view that the disease is the result of a deficiency of some nutritive factor in the diet. From this standpoint we may speak of the lack of an antiscorbutic vitamin, just as the lack of an antineuritic vitamin is postulated in the genesis of polyneuritis.[3]

[1] From the *Jour. Amer. Med. Asso.*, July 26, 1919.

[2] Holst and Frolich: *Ztschr. f. Hyg.*, 72: 1, 1912; 75: 334, 1913.

[3] Hess, A. F., and Unger, L. J.: Scurvy, VIII: Factors Affecting the Antiscorbutic Value of Food, *Am. J. Dis. Child.*, 17: 221 (April), 1919. Hart,

The lack of knowledge of the distribution of antiscorbutic vitamins has been accentuated by the needs of infant feeding. The use of cow's milk pasteurized at a temperature as low as 63° C. (145.4° F.) for thirty minutes has led in the course of several months to milk outbreaks of infantile scurvy,[4] thus indicating the poverty of heated milks in the antiscorbutic vitamin. Only recently Hart, Steenbock and Smith have demonstrated at the University of Wisconsin that milk sterilized at 120° C. for ten minutes, commercial unsweetened condensed milk, and the commercial milk powder examined had lost their antiscorbutic properties when used in quantities equivalent to an amount of raw milk which would prevent scurvy in guinea pigs on a diet of rolled oats and dried hay. From such citations it becomes evident why investigators of infant feeding have sought sources of antiscorbutics and why producers of food preparations are concerned with the retention of native antiscorbutic potency so far as this is possible. Recent writers[2] have sanely summarized the situation by saying that either the results with guinea pigs on experimental scurvy should not be translated to infantile scurvy, or we should follow the wiser course of using some antiscorbutic in conjunction with the exclusive use in infant feed of such heated milk products as have been described.

Thanks to the labor of a number of investigators both here and abroad, the pediatrician is no longer limited to the conventional orange juice in his efforts to avert scurvy in infants. Reference has been made in THE JOURNAL to some of the novelties, such as the raw juice of the swede and the tomato, which are also available for human nutrition. Although the antiscorbutic value of fruit juices was recognized three hundred years ago, Alice Henderson Smith,[5] of the Lister Institute in London, has upset the traditional faith in lime juice, as the result of her historical studies. It appears that the juice used with good effect in the olden days was in reality ob-

E. B., Steenbock, H., and Smith, D. W.: Studies of Experimental Scurvy: Effect of Heat on the Antiscorbutic Properties of Some Milk Products, *J. Biol. Chem.*, 38: 305 (June), 1919.

[4] Hess, A. F., and Fish, Mildred: Infantile Scurvy: The Blood, the Blood Vessels and the Diet, *Am. J. Dis. Child.*, 8: 385 (Dec.), 1914. Hess, A. F.: Infantile Scurvy, III, Its Influence on Growth (Length and Weight), *ibid.*, 12: 152 (Aug.), 1916.

[5] Smith, A. H.: A Historical Inquiry into the Efficacy of Lime Juice for the Prevention and Cure of Scurvy, *J. Royal Army Med. Corps*, Feb. and Mar., 1919; *Lancet*, 2: 725 (Nov. 30), 1918.

tained from lemons and sweet limes, not from the West Indian sour limes. With the change to the sour limes has come a failure in antiscorbutic potency that was difficult to understand until it was demonstrated recently by experimental tests on animals that the sour lime of the West Indies (*Citrus medica-acida*) happens to have only one quarter of the antiscorbutic value of the lemon (*Citrus medica-limonum*). Lemon juice is easily available for the treatment of infantile scorbutus. Harden and Zilva[6] have further demonstrated that after removal of the free citric acid and other acids from lemon juice, the residue also retains its antiscorbutic activity; and in collaboration with Still[7] these investigators have, for the first time, clinically employed with success this antiscorbutic factor separated from the greater part of the inactive components in combination with which it occurs. The vitamin-containing product could be administered in large dosage after the refinement and the exclusion of extraneous substances. In fact, the lemon product was given in concentration at least double—in one case seven times—as strong as the form in which it occurs naturally in the foodstuff (lemon) from which it was obtained. The treatment was thus, so to speak, "intensive," reminding one of the seemingly potent therapeutic procedure of Hess, who introduced orange juice directly into the circulation of scorbutic infants.

There are indications that the potent fruit juices can be suitably preserved for clinical use. This is a matter of no little consequence in conserving products that do not come into the market with uniform frequency and at reasonable prices throughout the year. Harden and Robinson[8] have reported from London that the antiscorbutic principle in orange juice is not volatilized when the juice is distilled at 40° C. under reduced pressure. By evaporation of orange juice at 40° C. under reduced pressure, it is possible to obtain a solid residue which possesses in a very high degree the antiscorbutic value of the fresh juice. This value is not appreciably diminished when the substance is kept in a dry atmosphere at room temperature during six months. The prolonged heating to which

[6] Harden, A., and Zilva, S. S.: The Antiscorbutic Factor in Lemon Juice, *Biochem. J.*, 12: 259 (Oct.), 1918.

[7] Harden, A., Zilva, S. S., and Still, G. F.: Infantile Scurvy: The Antiscorbutic Factor of Lemon Juice in Treatment, *Lancet*, 1: 17 (Jan. 4), 1919.

[8] Harden, A., and Robinson, R.: The Antiscorbutic Properties of Concentrated Fruit Juices, *J. Royal Army Med. Corps*, Jan., 1919.

fruit juices are subjected in the usual processes for the manufacture of jams and jellies renders it unlikely that these would ever possess any considerable antiscorbutic value. Nevertheless, Harden and Robinson have found that by the use of the newer extremely rapid commercial processes of concentration without the application of high temperatures, fruit jellies can be prepared (from the apple, for example) which are by no means devoid of antiscorbutic potency, though this is of a different order from that characteristic of the orange and lemon. Surely there can no longer be any excuse for the failure to avert infantile scurvy, even when fresh, unheated milk is not available.

PRODUCTION OF GLYCERIN FROM MOLASSES.[1]

By Arthur R. Ling.

In view of the apparent close structural relationship between the monohexoses, glucose, fructose, etc., and glycerin, the conclusion seems justified that it ought to be possible to obtain the latter compound by the fermentation of these sugars under certain conditions with one of the saccharomycetes or yeasts. Nor is this mere speculation, for be it remembered that Pasteur in 1858 observed that glycerin and succinic acid, albeit in traces only, are invariable products of the so-called alcoholic fermentation of the sugars, and this is now a well-established fact. Moreover, there is every reason to believe that the glycerin at all events formed in this way owes its origin directly to the sugars and not to the secondary constituents always present in those fermentable liquids, worts, musts, etc., met with in commerce. In this connection it may be pointed out that F. Ehrlich showed in 1907 that the higher alcohols and esters present in fermented worts and musts are derived from the amino acids and not from the sugars. In 1909 he brought forward evidence that succinic acid is formed in the same manner.

Despite numerous attempts to obtain glycerin in such quantity by the fermentation of sugars that its production in this way would become commercially profitable, no success has up to quite recently been met with.

[1] Reprinted from the *Journal of the Society of Chemical Industry*, May 21, 1919.

A report from the Laboratory of the Internal Revenue Bureau, Washington, dated May 6, 1918, has within the past few days been placed in the hands of the writer. In it experiments are described indicating that the problem of the production of glycerin by the fermentation of sugars in such a yield as to be of commercial significance has been solved.

It seems that Dr. Alonzo Taylor, then Assistant Secretary of Agriculture, reported that when in Germany in the summer of 1917 the Germans were producing glycerin in large quantities by a fermentation process. Investigations were undertaken at four different laboratories in the United States with a view to elucidating the problem, and Mr. A. B. Adams, Chief Chemist of the Laboratory of the Internal Revenue Bureau, Washington, was able to report to the Hon. Daniel C. Roper, Commissioner of Internal Revenue, three months after the work had been assigned to the laboratory, that Mr. John R. Eoff had solved the problem in so far that he was able to produce glycerin in such quantities that if the actual cost of the recovery was not too high the process would be commercially profitable. Details of the process have been furnished to the British and French authorities, and to interested manufacturers in the United States.

The report in which the experiments are described in detail is signed by Messrs. John R. Eoff, W. V. Linder and G. F. Beyer.

After numerous trials with pure cultures of different yeasts, *Saccharomyces ellipsoideus* (var. *Steinberg*), No. 657 of the collection of the American Museum of Natural History, New York, was selected as most suitable. Preliminary experiments were then instituted which ultimately led up to the following general conclusions:

The best yields of glycerin were obtained by fermenting solutions of sugar containing 5 per cent. of sodium carbonate, which must not be added to the liquid all at once. A less quantity of the alkali diminishes the yield of glycerin, while a larger quantity stops fermentation. Other alkaline substances, sodium hydroxide, potassium hydroxide, and borax may be used, but sodium carbonate (soda ash) is preferable on account of its cheapness. Although no hard and fast rule can be laid down for the method of adding the sodium carbonate, which must be varied according to the nature of the sugar solution, it should be added as soon as the fermentation has well started, and in as large quantities and as frequently as is

possible without stopping fermentation. The earlier the addition of the alkali, the higher the yield of glycerin will be. It is necessary that the yeast be "worked up" by making a "bub," and it has been observed that the presence of ammonium chloride in the fermenting liquid augments the yield of glycerin. The most favorable temperature for the fermentation is 30–32° C., and the fermenting liquid should not vary from these limits of temperature for any considerable period. Higher temperatures lead to a loss of alcohol and glycerin, and to the formation of objectionable substances, whilst smaller yields of glycerin are obtained at lower temperatures. The most favorable concentration for the sugar solutions lie between 17.5 and 20 Gms. of sugar per 100 Cc. It has been found that when fermentation is complete according to the method above outlined, 20–25 per cent. of the sugar originally present in the liquid is converted into glycerin, and practically all the remainder into alcohol and carbon dioxide. The nature of other substances which are formed has not yet been determined. It is mentioned that when the sodium carbonate has been added to the fermenting solution in sufficient quantity, a copious precipitate is formed, the evolution of gas ceases, and the yeast apparently lies dormant for a while. The precipitate eventually disappears and the fermentation again proceeds. It is essential that this precipitate should form, and that the fermenting liquid lie quiescent for a while. The addition of the sodium carbonate in solid form has been found to produce better results than if it be added in the form of a solution.

A description is next given of the process as carried out on a commercial scale, using inedible "black strap" Porto Rico molasses.

The yeast starter or "bub" is first prepared in the following manner. Yeast No. 657 (see above) was seeded with a platinum loop into 150 Cc. of sterile grape juice, and allowed to ferment to the final degree. Fifteen Cc. of this was then added to 150 Cc. of sterile grape juice, and when fermentation had finished 75 Cc. was added to 800 Cc. of a solution of sterilized "black strap" molasses at 21.2° Balling (about sp. gr. 1.085). As soon as brisk fermentation had set in, 3 Gms. of soda ash was added and the bottle shaken until solution was complete. After fermentation had resumed, and when it had reached its final point, the whole of the liquid was added to 2 gallons[2] of a similar "black strap" molasses solution,

[1] The gallon referred to in this article is the U. S. gallon. The factor for the conversion into the British gallon is 0.834.

and this was treated at the proper time with soda ash in the same proportion as before. Fermentation being complete, the whole two gallons was added to 40 gallons of a solution made as follows:

"Black strap" molasses was dissolved in sufficient water to make 425 gallons of wash at 21.2° Balling at 25° C. Eight pounds of ammonium chloride was added, and after the liquid had been sterilized sufficient sterile water was added to bring it back to the original density. This solution contained 16.85 per cent. of sugar. The following are the details of the main fermentation:

17.11.17., 9 A.M.—40 gallons of wash (see above) seeded (see above).

3 P.M.—2 lb. soda ash added.

9.15 P.M.—The 40 gallons added to 385 gallons molasses wash.

18.11.17., 12.30 A.M.—Added 24 lb. soda ash (T. 30° C.).

3.30 A.M.—Added 36 lb. soda ash (T. 31.5° C.).

5.30 A.M.—Added 48 lb. soda ash (T. 33° C. Attemperated to 30° C.).

11 A.M.—Added 48 lb. soda ash (T. 32.5° C. Attemperated to 30° C.).

5.30 P.M.—Added 36 lb. soda ash (T. 32° C. Attemperated to 30° C.).

The fermentation was then allowed to proceed to completion, which took five days, the temperature being kept at about 30° C.

At the conclusion of fermentation the wash was analyzed and the following results were obtained: Glycerin, 3.1 per cent. by vol.; alcohol, 6.75 per cent. by vol.; sugar (apparent), 0.86 per cent. by vol.; alkalinity, 3.6 Gms. Na_2CO_3 per 100 Cc.

The purification of the fermented wash was then carried out as follows: 3,200 lb. of the wash was neutralized in a tank with sulphuric acid, and 12 gallons of a saturated solution of commercial ferrous sulphate (copperas) added. The wash having been brought to near the boiling point, milk of lime was added until there was an excess of lime in solution, when the wash was boiled for half an hour by means of a steam coil. The liquid was next passed through a filter press, and the cake steamed. The copperas and lime treatment was then repeated, and after again being passed through a filter press the alkalinity was brought to 0.2 per cent. (Na_2CO_3) by the addition of soda ash. It was then filter pressed

and steamed, and the filtrate evaporated in a vacuum evaporator to a thick syrup which contained between 30 and 35 per cent. of glycerin. It was then distilled in a still resembling that of Jobbin. About 50 lb. of dynamite glycerin was thus obtained, or roughly about *half that present in the fermented wash.*

The following is an analysis of a sample of the dynamite glycerin:

Sp. gr. at 15.6° C., 1.2616; carbonaceous residue, 0.058 per cent.; ash, 0.009 per cent.

The carbonaceous residue is high, but a redistillation of the glycerin gave a satisfactory product. The glycerin was found to nitrate normally.

It is noteworthy that it has been found that the second treatment of the fermented wash with copperas and lime is superfluous. Hitherto it has not been found possible to obtain a perfect crude glycerin from molasses.

Several additional experiments have, it is stated, been carried out on a much larger scale—2,000 gallons—with the same results.

It will be remembered that in an earlier part of this report it was mentioned that from 20–25 per cent. of the sugar originally present in the mash is converted into glycerin. Taking the sugars actually fermented in "black strap" Porto Rico molasses as 50 per cent. of the molasses (and this is a very liberal estimate, for it may be computed from the figures given that nearly 3 per cent. of the sugar in the molasses is left unfermented), and remembering that only half the glycerin formed is recovered as crude glycerin, the yield of glycerin could not be expected to exceed 5½ to 6 lb. per cwt. of the molasses dealt with. It is only fair, however, to quote the following remarks of the signatories of the report. They say:

"It must be borne in mind that there is considerable alcohol produced in these fermentations. At the present price of alcohol and raw materials it is safe to say that the value of the alcohol balances the cost of all material and overhead charges entering into the production of the fermented mash. This being true, then the slop from the alcohol distillation which contains the glycerin is had free of cost, so that the only cost to be considered for the glycerin would be that of purification and distillation. This should not be great. No attempt has been made as yet to recover the alcohol, it being deemed a matter offering no difficulty."

Experiments have also been carried out on a large scale using cane sugar and starch glucose as fermentable material. It was found, however, necessary in these cases to employ yeast foods in quantities that deleteriously influenced the purification of the glycerin. It was therefore concluded that these materials possess no superiority over molasses for the purpose.

Since the process of producing glycerin by fermentation is in its present state of development restricted to molasses, the writer would point out that in some parts of the world, notably in Australia and Fiji, molasses is a waste product which is run out to sea. The present process should, therefore, be of great significance in such countries. There are several details in this process, as outlined in the report, which in the writer's opinion are open to criticism. As, however, a year has elapsed since the report was officially handed in, further developments may have eliminated the applicability of these criticisms.

COLLOIDAL METALS: THEIR PREPARATION AND PROPERTIES.[1]

By Thos. Stephenson, F.R.S. Edin.

The use of colloidal substances in medicine is of comparatively recent introduction, and now that knowledge of their properties and action is more exact, their employment in the treatment of disease is increasing rapidly. It is intended here to give merely a general sketch of the colloidal preparations in more general use: for details of the various varieties of colloids readers are referred to the very complete section on this subject in the Extra Pharmacopœia by Martindale and Westcott (16th edit., p. 308).

The term "colloid" (from κολλα, glue) was first used by Thomas Graham to distinguish those amorphous substances, of which glue and gelatin are typical examples, which diffuse with difficulty through membranes, as opposed to "crystalloids," which diffuse with ease. The word is now used to describe a condition which chemical substances may be made to assume, rather than to define a particular class of compounds. A colloidal solution is in reality a suspension of minute particles of the substance. These particles are

[1] Reprinted from *The Prescriber*, June, 1919.

charged with positive or negative electricity, and the passage of an electric current through the solution causes the particles to move respectively towards the cathode and the anode. Some colloidal solutions are readily precipitated by heat or by mechanical means, and, as will be seen later, this has to be guarded against in their therapeutic application.

The nature and properties of colloids and of colloidal solutions have been known for some time, but the assumption by the metals and metalloids of the colloidal state is a comparatively recent discovery. It is these that have come into extensive use in medicine. The first metal to be used in this way was colloidal silver, which, in 1896, was introduced into therapeutics under the name of "collargol." This substance, which occurs in small black scales having a metallic lustre, forms with water an opaque solution, which has all the properties of a colloid. Collargol, however, is not really a colloidal metal, but is generally considered to be a combination of an acid silver molecule with ammonia, *i. e.*, collargolate of ammonia.

Shortly after the introduction of collargol, Trillet succeeded in preparing oxydases of certain metals by precipitating solutions of metallic salts with an alkali in presence of albumin, forming a kind of colloidal solution of the metals. Later, Bredig produced the solutions known by his name. These are true colloidal "solutions" (or suspensions) of the metals, and are produced by passing an electric current through pure water between electrodes of the metal to be dissolved. The current diffuses a minute quantity of the metal throughout the liquid—the metal, in fact, becomes volatilized in the liquid. The resulting solution is in every case a dichroic liquid, transparent to transmitted light, and opaque to reflected light. Suspended particles can be detected only by the ultra-microscope, and the solution in all respects obeys the rules laid down for colloidal substances. The metal is in a state of very minute subdivision, and the particles possess that vibratory motion known as "Brownian movement." Different metals have been used in the preparation of such solutions, and more recently colloidal solutions of the metalloids, such as sulphur and iodine, have also been prepared.

In addition to the electrical method for the preparation of colloids, there is the chemical method which has come into fairly general use also. This usually consists in the reduction of a metallic salt by a suitable agent in the presence of a protective colloid such

as gelatin or gum, and the subsequent removal by dialysis of the by-products.

The great difficulty which attended the use of electrically-prepared colloids on their introduction was their instability. The particles had a natural tendency to agglutination, and, in consequence, the solution did not remain therapeutically active for more than a few hours. The usual methods of preservation appeared to be useless. Sterilization by heat caused the particles to agglutinate, and the same result followed the addition of a foreign substance, such as sodium chloride. When injected into the blood, the colloidal solution at once agglutinated, and any therapeutic action was consequently nullified. It was found, however, that the introduction of a small proportion of another colloid, such as gelatin or gum, prevented this agglutination, and the addition of such substance, known as a "protective colloid," has allowed of these preparations being preserved and isotonized for therapeutic use.

For a time it was thought that the therapeutic action of these colloidal solutions was merely catalytic or mechanical, but it is believed now that other factors are responsible. The results recorded of colloidal sulphur in the treatment of rheumatism; of colloidal silver in gonorrhœa; of colloidal antimony in kalaazar, all point to an intensification of the specific action of the metal, which is probably in the ionic condition. Be that as it may, the fact remains that whereas it was originally thought, and probably with some reason in the case of Bredig's solutions, that the actual metal employed was immaterial, it is now known that the different colloidal metals have different therapeutic effects, and cannot be employed indiscriminately.

Of the chemically produced colloids the principal are arsenic, antimony, copper ("cuprase"), gold, iodine, iron, mercury, platinum, selenium, silver, sulphur. "Oscols" and "collosols" are chemically prepared colloids, the names being the property of certain manufacturers.

Electrically produced colloids include copper, gold, mercury, selenium, silver, etc. The products on the market are styled "electr-,"—thus electragol (silver); electraurol (gold).

Under the name of "organosols," Martindale describes colloidal metals obtained by impregnation of lanolin with an aqueous solution of the salt of a heavy metal, and subsequent trituration with a

solution of alkali hydroxide. Double decomposition occurs, and the oxides or hydroxides of the heavy metals are obtained as colloids. The product may be dissolved in ether, in fats, or in liquid paraffin, the cholesterol acting as the protective agent.

Improvements in the preparation of colloidal metals for use in medicine are constantly being announced, and there is little doubt that these substances are destined to play an important part in therapeutics in the near future.

GERMAN POISON-GAS FACTORIES.[1]

The Allies in occupation of German territories have the right of access to the German chemical factories situated in the area, and an Inter-Allied Commission has visited the principal works devoted to the manufacture of dyes, medicinal products and standard chemicals. During the war these were occupied with the production of poison gas used in warfare. Major Theodore W. Sill, reporting on his visit as a representative of the United States on the Inter-Allied Commission, reports that, notwithstanding the air-raids to which the factories were subjected, these German plants, "probably the greatest of the potential possibilities for war-material production," are "in splendid condition with a large, highly trained force of employees, and, moreover, with additional opportunities for increasing their production by utilizing the extra equipment added for war-material production." The lack of oil and greases for lubrication of the machinery is the only apparent handicap in the factories. Major Sill warns the American people that this German industry is "a dangerous factor in the struggle for commercial supremacy, and also a potential source of war-material production unless properly controlled." The report (*Journal of Industrial and Engineering Chemistry*) then describes the visits paid to the various poison-gas factories.

"Arriving in Cologne, we made our headquarters there while making a tour of investigation through the plant of the Farbenfabriken vorm. Friedrich Bayer & Co. at Leverkusen, and also the plant of Weiler-ter-Meer at Uerdingen-on-the-Rhine.

"The plant of the Bayer Co. stands out preëminently as the best

[1] Reprinted from *The Chemist and Druggist*, June 28, 1919.

and most modern of German chemical plants. It is a veritable city in itself, well laid out, with excellently constructed streets and brick buildings. Their office building and recreation buildings for the employees are luxurious palaces. This plant has expanded considerably during the war, and, despite the contrary assertions of its directors, was widely engaged in the manufacture of war products, particularly poison gases. We had the opportunity of meeting Dr. Duisberg, the chief director, and incidentally, one of the ex-Kaiser's right-hand men in the development of the war. Many will remember him from his visit to this country at the time of the Chemical Congress in 1912. Incidentally, he hopes to be over here again very soon to see his 'old-time friends.'

"The plant of Weiler-ter-Meer at Uerdingen is also an excellent development, kept up in very good condition. . . . Of all the men whom we met in the various plants in Germany, the head of this plant was the most cordial and open in all his dealings with us. It was, of course, a difficult and humiliating position for men to be in, and in many cases we encountered sullen indifference, particularly among the plant directors, but among the lower classes of foremen and workmen there does not seem to be a general recognition of the fact that the war has been lost and also that the cause was wrong to start with. . . . After spending a few days in Coblenz . . . we journeyed up the Rhine to Mayence, the headquarters of the French area. Within this area we were privileged to visit the Kalle plant at Biebrich. Very little war work had been done at this place, and the plant was probably the poorest of all we saw, being old, dirty, and in a run-down condition.

"At Hoechst-on-the-Main we went through the great plant of Meister, Lucius and Brüning, who were the pioneers in the development of German poison gases, and had done considerable work in all kinds of war material. They, too, had a large, very fine plant, well laid out, and in good operating condition, extending for many acres along the river. They are quite progressive and have developed on a large scale.

"A little later we went up to the greatest of all plants, the Badische Anilin und Soda Fabrik at Ludwigshafen. This plant employs about 16,000 men and covers many acres of ground. They have the plant for dyestuffs, intermediates, etc., at Ludwigshafen, and a little further up the river, at Oppau, is located the plant for the Haber process. Considerable work on war products was done at Ludwigs-

hafen, but they also were able to make dyestuffs on an appreciable scale during the war. At the present time they have a large stock on hand ready to turn loose on the markets when permission is granted. They, too, had done considerable work on poison gases and explosive intermediates, but not to an extent which would at all interfere with their resumption of dyestuff manufacture on a large scale.

"At Oppau we saw what is probably the most phenomenal scientific development up to date—namely, the practical realization on an operating basis of the Haber process for ammonia production. The buildings are all quite new and well constructed, and the vast amount of detail has been studiously and carefully worked out on a practical operating basis, producing upward of 100,000 tons of ammonia per year. This plant was a large factor in enabling Germany to stay in the war as long as she did, by means of producing large quantities of nitrates. The Germans have also another plant, a duplicate of this, which they are operating in the unoccupied area of Germany, so that it is really a great practical possibility at the present time. Incidentally, it came to our attention that Haber, to whom Germany owes so much of her development in chemical products in warfare, had never attained a higher rank than captain in the German chemical warfare service, despite the responsibility and immensity of his job.

"Looking at our inspection of the German plants from a general viewpoint, it is my opinion that, considering the advantage gained in America by the last four years of experience in chemical manufacturing and the lessons learned by our equipment manufacturers, the German plants at the present time from an equipment standpoint and general layout are not superior to the existing American development, their advantage being that they have an experienced and long-trained personnel schooled and willing to carry on the laborious details; but if our people here at home will encourage our new, rapidly growing industries, there is no reason why our own personnel cannot equal or, in fact, surpass that of the Germans.

"There are but few distinctive features to be observed which might advantageously be adopted in some American plants. For instance—(1) the Germans have a very clever method of building their water-towers around the power-house chimneys or stacks, thus utilizing the waste heat and keeping their water from freezing; (2) they have a method of distributing the pressure in the filter presses

so that it is not only applied at the center by a large screw, as in most of our presses, but also horizontally along the sides of the press; (3) at one place we saw an excellent automatic nitration system, based upon the alternate filling and refilling of a small tank with a measured quantity of water, which in turn was connected with valves releasing definite amounts of acid and benzol; (4) the Germans have in practically all of their plants a very high grade of lead fittings, in which art they have advanced remarkably well; (5) in many cases it was also noted they used square flanges on the elbows for their high-pressure piping connections. On the other hand, one notices considerable lack of conveying equipment, such as bucket elevators and belt conveyors through these plants, the probability being that they utilize man power much more than we do, and do not rely upon mechanical equipment so much. . . .

"Among the developments to be noted during the war in Germany, which are of special interest, was the production of synthetic rubber on a large scale and a practical basis. This was done at the Bayer plant in Leverkusen, and the production, though very expensive, was of material assistance in meeting their great shortage of rubber."

URANIUM AS AN INDUSTRIAL POISON.[1]

Certain toxicologic effects of salts of uranium have long been recognized and applied in the study of experimental physiology and pathology. Recently industrial conditions have arisen which may place this element in the class of possible dangers of occupation. Karsner and his collaborators[2] of the Western Reserve University School of Medicine, Cleveland, have asserted that in certain industries uranium is employed or appears as a by-product, and that with war time scarcity of some other heavy metals, such as tungsten, uranium may be utilized as a partial substitute. In the production of radium, uranium oxide is produced in large quantities, and if

[1] Reprinted form the *Journal of the American Medical Association*, June 28, 1919.

[2] Karsner, H. T., and Reimann, S. P., "Studies of Uranium Poisoning, I. The Toxicity of Certain Water-Insoluble Salts of Uranium," *Jour. Med. Res.*, 39, 157 (Nov.), 1918. Karsner, H. T., Reimann, S. P., and Brooks, S. C., "Studies of Uranium Poisoning, II. The Solubility of Uranium Oxide in Artificial and Human Gastric Juice," *ibid.*, 39, 163, 169, 177 (Nov.), 1918.

uranium were employed in the steel industry the high temperatures used would lead to the formation of one or several oxides, the most important being uranium dioxide and uranous uranate, both of which are insoluble in water. In grinding, polishing, and perhaps in other operations, these oxides might appear in the form of a dust.

Animal experiments conducted by the Cleveland pathologists demonstrate that uranium oxide, the state in which the metal is most likely to reach the upper respiratory tract when distributed industrially in the form of dust, can be toxic and fatal when administered by mouth. This oxide is insoluble in water; but it will dissolve in gastric juice, so that the possibility of the formation of a soluble toxic salt is established. The production of nephritis by uranium salts has long been recognized as an experimental fact, and the method has served to facilitate the study of the pathology of renal functions. Karsner and his associates have observed that the excretion of uranium, so far as it is accomplished, is primarily by way of the kidneys. When functional and anatomic lesions arise in the kidneys through the presence of the poison, the decreased effectiveness of excretion makes matters worse by favoring an accumulation of the metal in the kidney. There is, probably, no special "affinity" of uranium for the kidney cells nor any unusual susceptibility to the poison on their part. The possibility of protecting the kidneys by the administration of alkalies to combat the concomitant acidosis in such cases represents one of the therapeutic considerations that experimental medicine has taught.[3]

Incidentally it should be stated that uranium nitrate was admitted to the Ninth (the most recent) Revision of the U. S. Pharmacopœia. Surely the danger of this salt could not have been appreciated when this action was taken by the Revision Committee. There does not appear to be sufficient evidence of its therapeutic value to warrant inclusion in this official book. The drug is not included in the Useful Drugs, prepared by the Council on Pharmacy and Chemistry. The Epitome of the U. S. Pharmacopœia, prepared for the use of physicians by a special committee of the Council on Pharmacy and Chemistry, has this to say under "Actions and Uses": "(Uranium nitrate) . . . has been used, without adequate justification, in the treatment of diabetes and cancer. Solutions are

[3] MacNider, W. deB., "The Inhibition of the Toxicity of Uranium Nitrate by Sodium Carbonate," *Jour. Exper. Med.*, 23, 171 (Feb.), 1916; "Relative Toxicity of Uranium Nitrate," *Jour. Exper. Med.*, 26, 1, 19 (July), 1917.

poisonous and produce glucosuria when injected subcutaneously, even in small doses." Our previous knowledge of this drug, now adequately supported by the work of Karsner, should lead the next Revision Committee to omit the drug from the Pharmacopœia.

DETOXICATED VACCINES.[1]

The living tissues of man and animals possess the inherent power of manufacturing specific antisubstances against germs when attacked by them. This peculiar power is so highly specialized that the antisubstance produced acts only against the infecting germ, and not against any other species. An "antigen" is a substance which, when injected into the living tissues, stimulates the production of an "antibody" towards itself. Each species of germ, alive or dead, is, therefore, a "specific antigen," for when the dead organisms—*i.e.*, a vaccine—are injected, the tissues immediately react and commence to manufacture at once the antisubstances which destroy the germ, or which neutralize the toxins it develops, and upon this action vaccine therapy is based. However, the germs are so toxic, either by reason of the exotoxins which they excrete, or of the endotoxins which remain enclosed within the stroma of the germ itself, that only small amounts of their dead bodies—*i.e.*, vaccine—could be injected, and so the amount of antisubstances produced was limited by the toxicity of the germ, thus limiting appreciably the effectiveness of vaccine therapy. To Captain David Thomson, R.A.M.C., belongs the honor of having made a discovery which may have far-reaching effects on the future of curative as well as preventive medicine, by increasing the effectiveness of vaccine therapy. In the course of his investigations[2] he found that the gonococcus was extremely soluble in a weak alkaline solution ($N/10$ or $N/20$ sodium hydroxide), but was entirely insoluble in weak acids. Further research showed that the meningococci, *B. typhosus*, *B. Friedlander* and *B. influenzæ* (Pfeiffer), were all very soluble in weak alkalies. On the other hand, Gram-positive organisms, such as staphylococci, streptococci, pneumococci, etc., resisted the action of N-sodium hydroxide solution. Further investigations led to the

[1] Reprinted from the *Chemist and Druggist*, July 5, 1919.

[2] *Lancet*, June 28, 1919.

discovery that when a $N/10$ alkaline solution of gonococci was precipitated by N-hydrochloric acid, the neutralized supernatant liquid was strongly toxic, and caused a severe reaction when injected subcutaneously; it was, indeed, more toxic than the actual precipitate of the gonococcus substance itself. All germs consist of stroma—*i.e.*, the framework of the organism—and toxin, produced by it. Both are soluble in alkali, but the stroma is precipitated on the addition of an acid, leaving the toxin in solution. The gonococcus, streptococcus, pneumococcus and *B. influenzæ* are very readily precipitated from their alkaline solution by acid. Captain Thomson has found that the toxin could be removed by simply washing the precipitate repeatedly with a weak acid, such as 0.5 per cent. acid sodium phosphate containing 0.5 per cent. carbolic acid. He prefers to inject the precipitate suspended in the above-mentioned solution to redissolving it in alkali and injecting this alkaline, or neutralized, solution. The use of detoxicated vaccines permits the injection of considerably larger doses than have hitherto been permissable. Apart from its great therapeutic significance, Captain Thomson's discovery of a method of detoxicating vaccines brings us a considerable step forward in elucidating the chemistry of bacilli and of their toxins, as the latter can now be isolated and studied.

PREPARATION OF ALGIN.

Chemists throughout the country will be interested to know that the Hercules Powder Company is devoting a good deal of attention to the extraction of algin from kelp. Algin is a substance whose properties are widely known, being a vegetable gum of extremely high viscosity. Its manufacture and use is on a firm footing in Europe, but so far the industry has never become well established in this country, largely, it is thought, because of difficulties in the way of securing a uniform supply of fresh kelp at a reasonable cost. The experience gained by the Hercules Powder Company in harvesting kelp for the manufacture of war materials has overcome these difficulties as far as this organization is concerned.

There is a wide field of possible usefulness for algin. Algin compounds in general give an exceedingly viscous solution, and for that reason their application as a sizing for textiles and paper, as a thickener for printing colors, and as a proofing for interior walls

and ceilings is at once apparent. The sodium compound of algin is soluble in water, a five per cent. solution thereof being so viscous that it can hardly be poured from a vessel. The compounds of the heavy metals with algin are insoluble in water, some of them being soluble in ammonia, which solvent is used in their application as a waterproofing material in textiles.

BOOK REVIEWS.

OPPORTUNITIES IN CHEMISTRY. By Ellwood Hendrick. 102 pages. 75 cents. Harper and Brothers, New York.

This is said to be "a book answering the first question of a man who thinks he wants to be a chemist. It tells him in simple straightforward language what possibilities chemistry offers and how to make a success of it."

The Introduction tells us that all of the good chemists known by the author have been full of curiosity, that the chemist must be imaginative, and, in order to have joy in chemistry, must be able to have "a good time by himself, just wondering, and thinking about things, and guessing out as best he can, how they happen." The author disavows any desire to advise men to take up chemistry as a means of support, but he strives to show men engaged in many varied lines of business how a knowledge of the chemistry of the things they handle may be a big asset to them.

He says "a knowledge of chemistry is something like a good wife. It will help a man along in his work, but he must not count on it to support him. We have not yet arrived at the time when chemistry is made as welcome as it should be. It is a good servant but a poor master, except to the man who is himself a master."

The book, which may be easily read in a couple of hours, contains many practical and interesting suggestions, both for the man whose knowledge of chemistry is nil and the one who is more or less familiar with the subject, and is written in a pleasing style.

It is a pity that preparation of copy and proofreading were not more carefully done, so that a number of errors—not very serious, it is true, but errors nevertheless—might have escaped appearing within the covers of the volume. Several of them are here noted.

On page 9, "sulphite (instead of sulphide) of Cadmium" is said

to be "used as a pigment." On pages 10 and 14, Cerium and Thorium, respectively (instead of their oxides), are said to be "used for incandescent gas mantles." On page 42, liquid air is said to be separated "by distilling off first the oxygen, then the nitrogen," when the reverse is the proper procedure, the author apparently overlooked the fact that nitrogen, which he says boils at — 194° C., is more volatile than oxygen, the boiling point of which he gives as — 182° C. On page 70, alcohol is said to be "a grand solvent for dissolving gums" and "it is an excellent disinfectant." Page 89 contains a statement with reference to the reaction which ensues when calcium phosphide and water are mixed which does not agree with general observations.

F. P. Stroup.